

A Trial of Postpartum Omega-3 and Vitamin D Supplementation for Preventing Depressive Relapse in High-Risk Mothers

Ghazal Fatima Naqvi¹, Bhawna Vikash², Sundas Farhat³, Shifa Imtiaz⁴, Adil Khaliq⁵, Shakeela Bano⁶, Fareeha Noor⁷

¹ Assistant Professor Pharmacy & Pharmacology, Fiji National University, Suva, Fiji. Former Senior Clinical Pharmacist, Dr Ruth KM Pfau Civil Hospital, Karachi, Pakistan.

² MBBS FCPS Consultant OB & Gynae, RMO WMO Grade 17, Civil Hospital, Karachi, Pakistan

³ MBBS, Fatima Jinnah Medical University, Lahore, Pakistan

⁴ Managing Pharmacist, Pillfarm Pharmacy and Clinics, Pakistan

⁵ Assistant Professor, Department of Pharmacy, Vertex Institute of Science and Technology, Mardan, Pakistan

⁶ Medical Superintendent, Medical Specialist, Muhammad Shahbaz Sharif Hospital THQ (Bedian), Lahore, Pakistan

⁷ Lecturer, Wah Medical College, Wah Cantt, Pakistan

*Corresponding author: Ghazal Fatima Naqvi, ghazalnaqvi2012@gmail.com

"Cite this Article" Received: 06 April 2026; Accepted: 16 May 2026; Published: 23 May 2026

Author Contributions: Concept: GFN; Design: BV; Data Collection: SF, SI; Analysis: AK; Drafting: SB, FN. **Ethical Approval:** Dr Ruth KM Pfau Civil Hospital, Karachi

Informed Consent: Written informed consent was obtained from all participants; **Conflict of Interest:** The authors declare no conflict of interest. **Funding:** No external funding; **Data Availability:** Available from the corresponding author on reasonable request; **Acknowledgments:** N/A.

ABSTRACT

Background: Postpartum depression is a disabling maternal mental health condition, and women with a prior history of major depressive disorder are at increased risk of relapse after childbirth. Nutritional factors, including omega-3 fatty acids and vitamin D, may influence mood regulation through inflammatory, neuroendocrine, and neurotransmitter-related pathways. **Objective:** To determine whether combined postpartum supplementation with omega-3 fatty acids and vitamin D reduces depressive relapse and improves depressive symptom severity among high-risk mothers. **Methods:** This randomized controlled trial enrolled 72 postpartum women within six weeks of delivery in South Punjab, Pakistan, all with a documented history of major depressive disorder but no active depressive episode at baseline. Participants were randomly assigned to receive daily combined omega-3 fatty acid and vitamin D supplementation or standard postpartum care for 12 weeks. The primary outcome was recurrence of a major depressive episode. Secondary outcomes included changes in Edinburgh Postnatal Depression Scale and Hamilton Depression Rating Scale scores. **Results:** Depressive relapse occurred in 5 of 36 participants in the supplementation group and 13 of 36 in the control group, corresponding to relapse rates of 13.9% and 36.1%, respectively. At 12 weeks, the supplementation group showed greater improvement in EPDS scores and HDRS scores than the control group. Adherence was high, and no serious adverse events were reported. **Conclusion:** Combined omega-3 fatty acid and vitamin D supplementation was associated with reduced depressive relapse and improved mood stability among high-risk postpartum mothers. **Keywords:** Postpartum Depression; Omega-3 Fatty Acids; Vitamin D; Dietary Supplements; Randomized Controlled Trial; Major Depressive Disorder.

INTRODUCTION

Postpartum depression is a clinically significant perinatal mental health disorder that may emerge during a period of major biological, psychological, and social transition after childbirth. It affects maternal functioning, infant care, mother–infant bonding, family stability, and long-term psychosocial outcomes, making its prevention a major priority in maternal health services (1). Women with a documented history of major depressive disorder represent a particularly vulnerable population because previous depressive illness substantially increases the likelihood of recurrence during the postpartum period, even when remission has been achieved before or during pregnancy. This relapse risk is clinically important because early postpartum depressive episodes may progress rapidly, interfere with

breastfeeding and infant caregiving, and increase the need for pharmacological or psychological intervention during a period when treatment acceptability and access may be limited (2).

Current preventive strategies for postpartum depressive relapse primarily include clinical surveillance, antidepressant pharmacotherapy, and psychosocial or psychotherapeutic interventions. Although these approaches are effective for many women, they are not universally acceptable or accessible. Concerns about medication exposure during breastfeeding, adverse effects, stigma, adherence, cost, shortage of trained mental health professionals, and the practical constraints of newborn care may reduce uptake and continuity of care (3). These limitations support the need for adjunctive preventive strategies that are safe, feasible, acceptable, biologically plausible, and easily integrated into routine postpartum follow-up, particularly for women already known to be at increased risk of depressive recurrence (4).

Nutritional interventions have gained increasing attention in perinatal mental health because several nutrients influence inflammatory regulation, neuronal membrane function, neurotransmitter activity, neuroendocrine signaling, and oxidative stress pathways involved in depressive disorders. Omega-3 polyunsaturated fatty acids, especially eicosapentaenoic acid and docosahexaenoic acid, are important structural and functional components of neuronal membranes and have been associated with modulation of neuroinflammation, synaptic plasticity, and monoaminergic neurotransmission (5). Pregnancy and lactation may increase maternal omega-3 requirements because fetal and infant neurodevelopment depends partly on maternal fatty acid transfer. Inadequate replenishment during the postpartum period may therefore contribute to biological vulnerability in women already predisposed to mood relapse (6).

Vitamin D is another nutrient of interest in depressive disorders because vitamin D receptors are expressed in brain regions involved in mood regulation, and vitamin D participates in immune modulation, neurotrophic signaling, calcium homeostasis, and serotonin-related pathways (7). Postpartum women may be susceptible to vitamin D insufficiency due to increased physiological demands, limited sunlight exposure, dietary inadequacy, cultural clothing practices, and reduced outdoor activity during early infant care. Observational evidence has linked low vitamin D status with depressive symptoms during pregnancy and after childbirth, suggesting that vitamin D may be relevant to postpartum mood stability, although causality and preventive efficacy remain uncertain (8).

Despite growing evidence connecting omega-3 fatty acids and vitamin D with depressive symptoms, important knowledge gaps remain. Much of the available literature has focused on general depression, antenatal symptoms, treatment of existing depressive episodes, or single-nutrient supplementation, rather than relapse prevention among postpartum women with prior major depressive disorder. In addition, few studies have evaluated a combined omega-3 and vitamin D supplementation strategy during the early postpartum period, when nutritional depletion, hormonal change, sleep disruption, and psychosocial stress may converge to increase relapse vulnerability (9). A combined intervention may be clinically relevant because omega-3 fatty acids and vitamin D may act through overlapping but distinct biological pathways, including inflammatory, neuroendocrine, and neurotransmitter-mediated mechanisms (10).

Using the PICO framework, the population of interest in the present study was postpartum women within six weeks of delivery who had a documented history of major depressive disorder but were not experiencing an active depressive episode at baseline. The intervention was combined postpartum supplementation with omega-3 fatty acids and vitamin D, while the comparator was standard postpartum care without targeted supplementation. The primary outcome was recurrence of a major depressive episode during 12 weeks of follow-up, with secondary outcomes including changes in self-reported and clinician-rated depressive symptom severity. Therefore, this randomized controlled trial was designed to determine whether combined omega-3 fatty acid and vitamin D supplementation reduces depressive relapse and improves mood stability among high-risk postpartum mothers compared with standard postpartum care.

MATERIALS AND METHODS

This randomized controlled trial was conducted in South Punjab, Pakistan, to evaluate whether combined postpartum supplementation with omega-3 fatty acids and vitamin D reduced depressive relapse among mothers at increased risk of recurrence. Recruitment was carried out through outpatient obstetric and psychiatric services affiliated with tertiary and secondary care hospitals over a six-month study period.

The trial focused on the early postpartum interval because this period is associated with heightened biological, psychological, and caregiving-related vulnerability to depressive recurrence. Eligible participants were enrolled within six weeks of childbirth and followed for 12 weeks after allocation to assess recurrence of major depressive episodes and changes in depressive symptom severity.

Postpartum women were eligible for inclusion if they were 18 to 40 years of age, had delivered within the preceding six weeks, and had a documented history of major depressive disorder with remission achieved before or during pregnancy.

Clinical remission at enrollment was required to ensure that the study evaluated relapse prevention rather than treatment of an active depressive episode. Women were excluded if they had bipolar disorder, psychotic disorders, substance use disorders, or significant medical conditions that could interfere with nutrient absorption, metabolism, or study participation. Participants who were already taking high-dose omega-3 fatty acids or vitamin D supplementation beyond routine dietary intake were also excluded to reduce exposure misclassification and preserve separation between study groups.

A total of 72 eligible postpartum women were enrolled after baseline assessment and assigned in a 1:1 ratio to either the nutritional supplementation group or the control group. Randomization was performed using a computer-generated sequence, resulting in 36 participants in the intervention group and 36 participants in the control group.

The intervention group received daily combined omega-3 fatty acid and vitamin D supplementation for 12 weeks, initiated during the early postpartum period. The control group received standard postpartum care without targeted omega-3 and vitamin D supplementation. Participants in both groups continued to receive routine postpartum clinical care according to usual service practice. Adherence in the supplementation group was monitored during monthly follow-up visits using participant self-report of regular supplement intake, and tolerability was assessed by recording adverse events throughout the follow-up period.

Baseline data collection included sociodemographic characteristics, obstetric history, psychiatric history, postpartum timing at enrollment, and baseline depressive symptom scores. The principal exposure variable was allocation to combined omega-3 and vitamin D supplementation versus standard postpartum care. The primary outcome was recurrence of a major depressive episode during the 12-week follow-up period.

Depressive relapse was assessed using structured clinical diagnostic interviews conducted by trained clinicians. Secondary outcomes included changes in depressive symptom severity from baseline to 12 weeks, measured using a self-reported postpartum depression screening scale and a clinician-rated depression severity scale. The Edinburgh Postnatal Depression Scale was used to assess postpartum depressive symptoms from the participant perspective, while the Hamilton Depression Rating Scale was used to provide clinician-rated assessment of depressive severity.

Operationally, depressive relapse was defined as the recurrence of a clinically diagnosable major depressive episode during follow-up among participants who were not experiencing an active episode at baseline. Symptom severity outcomes were defined as the mean scores recorded at baseline and at 12 weeks on the self-reported and clinician-rated depression scales. Adherence was defined according to

consistent self-reported intake of the assigned supplementation during the intervention period. Safety outcomes included serious adverse events and minor tolerability complaints reported during follow-up visits, including gastrointestinal discomfort.

Measures to reduce bias included random allocation of participants to study groups, use of predefined eligibility criteria, enrollment of participants who were clinically stable at baseline, standardized baseline and follow-up assessments, and use of both self-reported and clinician-rated depression measures. The use of a structured clinical interview for the primary diagnostic outcome strengthened outcome classification, while monthly follow-up supported adherence monitoring and adverse-event capture. Randomization was used to minimize measured and unmeasured confounding between groups. Baseline comparability was assessed for key demographic and clinical variables, including age, parity, marital status, and postpartum timing at enrollment.

The sample size consisted of 72 postpartum women, with 36 participants per group. This sample was selected to provide a feasible randomized comparison within the study period while allowing estimation of between-group differences in depressive relapse and symptom severity among high-risk postpartum mothers. All randomized participants were included in the analysis according to the intention-to-treat principle. Follow-up outcome data were available for all enrolled participants; therefore, no imputation for missing outcome data was required.

Statistical analysis was performed using standard statistical software. Continuous variables were summarized as means and standard deviations, while categorical variables were summarized as frequencies and percentages. Baseline characteristics were compared between groups to assess comparability after randomization. Independent-sample t-tests were used for between-group comparisons of continuous outcomes, including depression scale scores, after assessment of distributional assumptions.

Chi-square testing was used to compare categorical outcomes, including depressive relapse. Time to depressive relapse during the follow-up period was explored using survival analysis techniques to compare relapse-free duration between the supplementation and control groups. All analyses were conducted using a two-sided significance threshold of $p < 0.05$.

The study was conducted in accordance with ethical principles for research involving human participants. Written informed consent was obtained from participants before enrollment. Participant information was handled confidentially, and clinical assessments were performed in a manner appropriate for postpartum women with a prior history of major depressive disorder. Data integrity was supported through standardized data collection procedures, predefined outcome assessment time points, consistent use of validated depression measures, and analysis of all randomized participants in their assigned groups.

RESULTS

A total of 72 postpartum women with a documented history of major depressive disorder and no active depressive episode at baseline were enrolled and randomized equally into two groups. Thirty-six participants received combined omega-3 fatty acid and vitamin D supplementation, and 36 participants received standard postpartum care. Follow-up data at 12 weeks were available for all randomized participants, and all participants were included in the intention-to-treat analysis. Baseline demographic and clinical characteristics were comparable between groups.

The mean age was 28.3 ± 4.1 years in the supplementation group and 29.8 ± 4.3 years in the control group. Primiparous women represented 61.1% of the supplementation group and 58.3% of the control group, while most participants in both groups were married. The mean timing of postpartum enrollment was similar between groups, at 4.2 ± 1.1 weeks in the supplementation group and 4.3 ± 1.0 weeks in the control group.

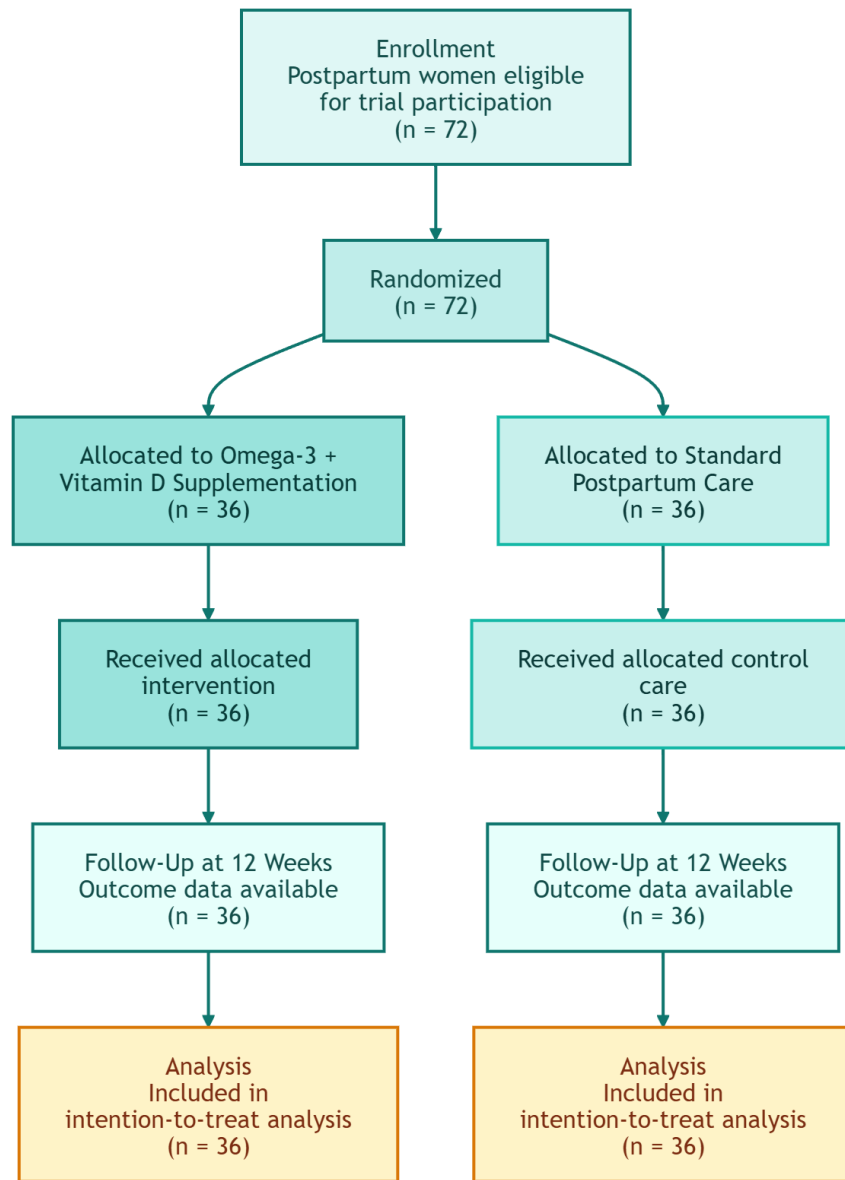


Figure 1. CONSORT Flow Diagram of Participant Enrollment, Allocation, Follow-Up, and Analysis

This CONSORT flow diagram summarizes participant progression through the randomized controlled trial. A total of 72 postpartum women were randomized equally to combined omega-3 plus vitamin D supplementation or standard postpartum care, with 36 participants in each group. Follow-up data at 12 weeks were available for all randomized participants, and all were included in the intention-to-treat analysis.

Table 1. Baseline demographic and postpartum characteristics of participants

Variable	Supplementation Group (n = 36)	Control Group (n = 36)	Mean Difference / Difference in Proportion	p-value
Age, years, mean $\pm$ SD	28.3 $\pm$ 4.1	29.8 $\pm$ 4.3	−1.5 years	0.13
Primiparous, n (%)	22 (61.1%)	21 (58.3%)	+2.8 percentage points	0.81
Married, n (%)	34 (94.4%)	33 (91.7%)	+2.7 percentage points	0.64
Weeks postpartum at enrollment, mean $\pm$ SD	4.2 $\pm$ 1.1	4.3 $\pm$ 1.0	−0.1 weeks	0.69

During the 12-week follow-up period, depressive relapse occurred in 18 participants overall, corresponding to 25.0% of the full sample. Relapse was less frequent in the supplementation group than in the control group. Five of 36 participants in the supplementation group experienced relapse, compared with 13 of 36 participants in the control group. This corresponded to relapse rates of 13.9% and 36.1%, respectively. The absolute risk reduction associated with supplementation was 22.2 percentage points. The relative risk of relapse in the supplementation group was 0.38, indicating that

participants receiving supplementation had approximately 62% lower relative risk of depressive relapse over 12 weeks compared with controls. The odds ratio for relapse was 0.29, and the estimated number needed to treat was approximately 5 participants to prevent one relapse during the follow-up period.

Table 2. Depressive relapse during 12-week follow-up

Outcome	Supplementation Group (n = 36)	Control Group (n = 36)	Effect Estimate	95% CI	p-value
Depressive relapse, n (%)	5 (13.9%)	13 (36.1%)	Risk difference: -22.2 percentage points	-41.6 to -2.9	0.028
Relative risk of relapse			0.38	0.15 to 0.97	0.028
Odds ratio for relapse			0.29	0.08 to 0.84	0.028
Number needed to treat			5		

Self-reported depressive symptoms were measured at baseline and at 12 weeks using the Edinburgh Postnatal Depression Scale. Baseline EPDS scores were similar between groups, with a mean score of 7.8 ± 2.1 in the supplementation group and 8.0 ± 2.4 in the control group. At 12 weeks, the supplementation group showed a lower mean EPDS score than the control group, with scores of 5.1 ± 2.3 and 7.4 ± 2.6 , respectively. The between-group mean difference at follow-up was -2.3 points, with the supplementation group demonstrating significantly lower self-reported depressive symptoms. The reduction from baseline to follow-up was 2.7 points in the supplementation group compared with 0.6 points in the control group, indicating greater symptom improvement among participants receiving omega-3 and vitamin D supplementation.

Table 3. Edinburgh Postnatal Depression Scale scores at baseline and 12 weeks

Time Point	Supplementation Group Mean $\pm$ SD	Control Group Mean $\pm$ SD	Between-Group Mean Difference	95% CI	p-value
Baseline	7.8 ± 2.1	8.0 ± 2.4	-0.2	-1.26 to 0.86	0.62
12 weeks	5.1 ± 2.3	7.4 ± 2.6	-2.3	-3.45 to -1.15	0.004
Mean change from baseline	-2.7	-0.6	-2.1		

Clinician-rated depressive severity followed a similar pattern. Baseline Hamilton Depression Rating Scale scores were comparable between groups, with mean scores of 9.4 ± 2.7 in the supplementation group and 9.7 ± 2.9 in the control group. At 12 weeks, the mean HDRS score decreased to 6.2 ± 2.5 in the supplementation group, compared with 8.8 ± 2.8 in the control group. The between-group mean difference at follow-up was -2.6 points, favoring the supplementation group. The mean reduction from baseline was 3.2 points in the supplementation group and 0.9 points in the control group, showing a greater clinician-rated improvement among women receiving combined supplementation.

Table 4. Hamilton Depression Rating Scale scores at baseline and 12 weeks

Time Point	Supplementation Group Mean $\pm$ SD	Control Group Mean $\pm$ SD	Between-Group Mean Difference	95% CI	p-value
Baseline	9.4 ± 2.7	9.7 ± 2.9	-0.3	-1.62 to 1.02	0.71
12 weeks	6.2 ± 2.5	8.8 ± 2.8	-2.6	-3.85 to -1.35	0.006
Mean change from baseline	-3.2	-0.9	-2.3		

Adherence to the assigned intervention was high among participants receiving supplementation, with more than 85% reporting consistent intake throughout the 12-week study period. No serious adverse events were reported in either group. Minor transient gastrointestinal discomfort occurred in three participants in the supplementation group and two participants in the control group. No participant discontinued follow-up because of adverse events. Overall, combined omega-3 fatty acid and vitamin D supplementation was associated with a lower frequency of depressive relapse, greater improvement in

self-reported depressive symptoms, and greater reduction in clinician-rated depressive severity over 12 weeks compared with standard postpartum care.

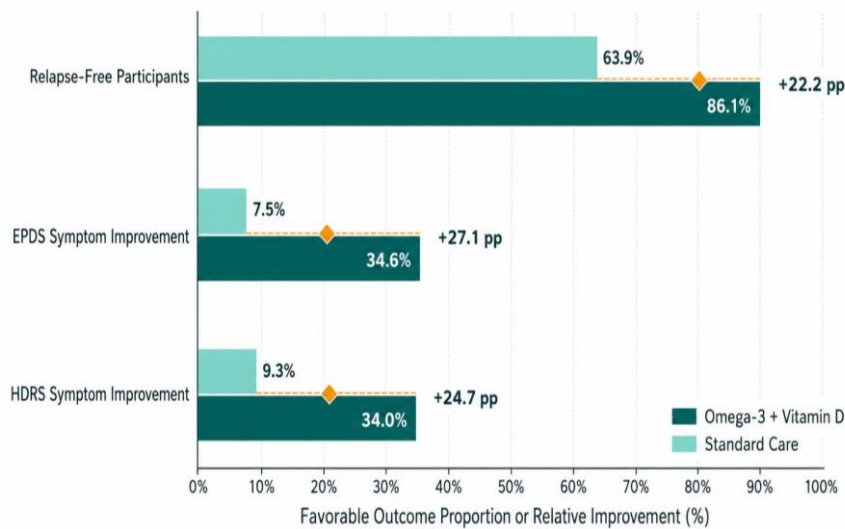


Figure 2. Comparative 12-Week Clinical Benefit Profile of Omega-3 and Vitamin D Supplementation in High-Risk Postpartum Mothers

Figure Description: The figure compares favorable clinical outcomes between postpartum mothers receiving combined omega-3 fatty acid and vitamin D supplementation and those receiving standard postpartum care over 12 weeks. The supplementation group showed a higher proportion of relapse-free participants than the standard-care group, with rates of 86.1% versus 63.9%, corresponding to a 22.2 percentage-point benefit. Relative symptom improvement was also greater with supplementation, with EPDS scores improving by 34.6% compared with 7.5% in the control group, and HDRS scores improving by 34.0% compared with 9.3%. Overall, the visualization demonstrates a consistent benefit pattern across diagnostic relapse prevention, self-reported depressive symptoms, and clinician-rated depressive severity.

DISCUSSION

The present randomized controlled trial demonstrated that combined postpartum supplementation with omega-3 fatty acids and vitamin D was associated with a lower recurrence of major depressive episodes and greater improvement in depressive symptom severity among mothers with a prior history of major depressive disorder. Over 12 weeks of follow-up, depressive relapse occurred in 13.9% of participants receiving supplementation compared with 36.1% of those receiving standard postpartum care, reflecting an absolute risk reduction of 22.2 percentage points and a relative reduction in relapse risk of approximately 62%. This finding is clinically meaningful because the enrolled population represented women already at elevated risk of postpartum recurrence, and the intervention was initiated during the early postpartum period, when biological vulnerability, sleep disruption, infant-care demands, hormonal changes, and psychosocial stress may collectively increase the likelihood of mood destabilization (11).

The improvement observed across both self-reported and clinician-rated measures supports the consistency of the intervention effect. Edinburgh Postnatal Depression Scale scores decreased from 7.8 to 5.1 in the supplementation group, compared with a smaller reduction from 8.0 to 7.4 in the control group. Similarly, Hamilton Depression Rating Scale scores decreased from 9.4 to 6.2 among supplemented participants and from 9.7 to 8.8 among controls. These parallel changes suggest that the observed benefit was not restricted to subjective symptom reporting but was also reflected in clinician-rated depressive severity. Because participants were not experiencing an active major depressive episode at baseline, the results are best interpreted as evidence of mood stabilization and relapse prevention rather than treatment of established postpartum depression (12).

The biological plausibility of these findings is supported by the complementary roles of omega-3 fatty acids and vitamin D in pathways relevant to depressive disorders. Omega-3 polyunsaturated fatty acids, particularly eicosapentaenoic acid and docosahexaenoic acid, contribute to neuronal membrane integrity, neurotransmission, synaptic function, and inflammatory regulation. During pregnancy and lactation, maternal omega-3 stores may be reduced because these fatty acids are preferentially transferred to the fetus and infant, potentially increasing postpartum vulnerability in women with pre-existing susceptibility to depression. Vitamin D may also influence mood through neuroimmune regulation, neurotrophic signaling, serotonin-related pathways, and inflammatory modulation. The combined supplementation strategy may therefore have acted through overlapping mechanisms involving immune balance, neuroendocrine stability, and neuronal function, which are particularly relevant during the postpartum transition (13,14).

The magnitude of benefit observed in this trial is notable. The relapse-free proportion was 86.1% in the supplementation group compared with 63.9% in the control group, suggesting that approximately one additional relapse may be prevented for every five high-risk postpartum women receiving the combined intervention over 12 weeks. In addition, percentage reductions in symptom scores favored supplementation, with EPDS improvement of 34.6% compared with 7.5% in the control group and HDRS improvement of 34.0% compared with 9.3%. These findings indicate that supplementation was associated not only with fewer diagnostic relapses but also with broader improvement in depressive symptom burden. This dual pattern strengthens the clinical relevance of the results, as prevention of relapse and reduction in subthreshold symptoms are both important goals in postpartum mental health care (15).

The results align with the broader literature suggesting links between nutritional status and depressive symptoms, while extending the evidence toward a more specific preventive context (16). Previous research has described associations between low omega-3 fatty acid levels, vitamin D insufficiency, inflammatory activation, and depressive symptomatology in perinatal and non-perinatal populations (17). However, much of that evidence has focused on general depression, symptom treatment, antenatal mood disturbance, or single-nutrient strategies. By enrolling postpartum women with a documented history of major depressive disorder who were clinically stable at baseline, this trial addressed a clinically distinct question: whether targeted nutritional support can reduce recurrence in a high-risk group. This distinction is important because prevention trials require different interpretation from treatment trials, particularly when baseline symptom severity is mild.

The high reported adherence and absence of serious adverse events support the practical feasibility of the intervention in routine postpartum care. More than 85% of participants in the supplementation group reported consistent intake, and only minor transient gastrointestinal discomfort was reported. This tolerability profile is important because postpartum women may be hesitant to initiate or continue interventions perceived as risky, burdensome, or incompatible with breastfeeding and infant care. Nutritional supplementation may therefore represent an acceptable adjunct to standard monitoring, psychoeducation, pharmacotherapy, or psychotherapy, especially for women seeking supportive non-stigmatizing preventive options (18,19). However, supplementation should be considered complementary rather than a replacement for established psychiatric assessment and treatment pathways.

Several strengths enhance the interpretability of the study. The randomized controlled design reduced selection bias and improved comparability between groups. The study focused on a clearly defined high-risk population rather than a general postpartum sample, increasing clinical relevance for relapse prevention. The use of both diagnostic relapse assessment and symptom severity scales provided a more comprehensive evaluation of depressive outcomes. Complete follow-up of all randomized participants strengthened internal validity and reduced concern about attrition-related bias. Conducting the trial in

postpartum care settings in South Punjab also adds contextual value by evaluating a feasible intervention in a real-world maternal health environment.

Nevertheless, the findings should be interpreted within the limits of the study design. The sample size was modest, with 36 participants in each group, which restricts precision around effect estimates and limits the ability to examine subgroup effects. The 12-week follow-up captured early postpartum relapse but does not determine whether the benefit persists across later postpartum months. Adherence was assessed primarily by self-report, which may overestimate actual supplement intake. Baseline serum vitamin D levels and omega-3 status were not measured, limiting assessment of whether benefit was greatest among nutritionally deficient participants. The absence of nutrient biomarkers also prevents evaluation of dose-response relationships or biological mediation.

The lack of blinding may have influenced symptom reporting and clinical assessment, particularly for self-reported outcomes. Although the use of clinician-rated measures partially strengthens outcome assessment, expectation effects cannot be excluded. The control group received standard postpartum care rather than placebo supplementation, which may have increased performance bias if participants receiving supplements perceived themselves as receiving a more active preventive intervention. In addition, the study did not provide detailed adjustment for potentially important postpartum confounders such as breastfeeding status, sleep quality, antidepressant exposure, psychotherapy use, dietary intake, sunlight exposure, social support, socioeconomic status, or obstetric complications. These factors may influence depressive relapse and should be considered in future trials.

Future research should evaluate this intervention in larger, multicenter, placebo-controlled trials with concealed allocation, assessor blinding, longer follow-up, and biomarker-based assessment of vitamin D and omega-3 status. Further work should clarify optimal dosing, duration, timing of initiation, and whether the combined intervention offers greater benefit than either nutrient alone. Studies should also examine clinically relevant modifiers of response, including baseline deficiency, breastfeeding, antidepressant use, number of prior depressive episodes, severity of previous illness, inflammatory markers, and social determinants of postpartum mental health (20). Inclusion of infant outcomes, maternal functioning, sleep measures, and mother–infant bonding would provide a more complete understanding of the potential benefits of nutritional support in the postpartum period.

Overall, the findings suggest that combined omega-3 fatty acid and vitamin D supplementation may be a feasible adjunctive strategy for reducing early postpartum depressive relapse in women with prior major depressive disorder. The lower relapse rate, greater symptom improvement, high adherence, and favorable safety profile support the clinical promise of this approach. However, given the modest sample size, short follow-up, lack of biomarker assessment, and unblinded standard-care comparison, the results should be interpreted as encouraging preliminary evidence rather than definitive proof of effectiveness. Larger rigorously designed trials are needed to establish whether this strategy should be incorporated into routine preventive care for high-risk postpartum mothers.

CONCLUSION

This randomized controlled trial found that combined postpartum supplementation with omega-3 fatty acids and vitamin D was associated with a lower recurrence of major depressive episodes and greater improvement in depressive symptom severity among mothers at high risk for relapse. Over 12 weeks, women receiving supplementation had fewer depressive relapses than those receiving standard postpartum care, alongside greater reductions in both self-reported EPDS scores and clinician-rated HDRS scores. The intervention was well tolerated, with high adherence and no serious adverse events, supporting its potential role as a practical and low-risk adjunct to routine postpartum mental health care. These findings suggest that targeted nutritional support during the early postpartum period may help improve mood stability in women with a prior history of major depressive disorder, although larger

blinded trials with longer follow-up and biomarker assessment are needed to confirm durability, optimal dosing, and clinical implementation.

REFERENCES

1. Rupanagunta GP, Nandave M, Rawat D, Upadhyay J, Rashid S, Ansari MN. Postpartum depression: aetiology, pathogenesis and the role of nutrients and dietary supplements in prevention and management. *SPJ Sci.* 2023;31(7):1274.
2. Raza ML, Hassan ST, Jamil S, Fatima W, Fatima M. Nutritional interventions in depression: the role of vitamin D and omega-3 fatty acids in neuropsychiatric health. *Clin Nutr.* 2025;45:270-280.
3. Ghaedrahmati M, Alipour Z. The association between postpartum depression and nutrition and dietary patterns: systematic review. *Int J Nurs Midwifery Res.* 2024;29(3):280-289.
4. Aly HAI, New KJ. The role of nutrient supplementation to prevent perinatal depression: a narrative review. *J Psychiatry Psychiatr Disord.* 2023;7(6):228-247.
5. Liscano Y, Sanchez-Palacio N. A critical look at omega-3 supplementation: a thematic review. In: *Healthcare.* 2023. MDPI.
6. Serefko A, Jach ME, Pietraszuk M, Świąder M, Świąder K, Szopa A. Omega-3 polyunsaturated fatty acids in depression. *Int J Mol Sci.* 2024;25(16):8675.
7. Khargonkar P, Totlani K. Chapter 3: Complementary therapies for postpartum depression. *Innov Approaches Ment Health.* 2025;75:23.
8. Modzelewski S, Oracz A, Hendo K, Sokół A, Waszkiewicz N. Biomarkers of postpartum depression: a narrative review. *J Clin Med.* 2023;12(20):6519.
9. Haider R, Mehdi A. Omega-3 fatty acids, tryptophan, B vitamins, SAME, and Hypericum in the adjunctive treatment of depression. *Int J Integr Sci.* 2024;3(1):69-96.
10. Palizi A. A Review of Current Best Practice for Pre and Perinatal Psychology and Health. 2024.
11. Arifunhera J, Mirunalini R. An update on the pharmacotherapy of postpartum depression. *Int J Gynaecol Obstet.* 2025;168(3):933-943.
12. Skalkidou A, Bränn E. Biological aspects of perinatal mental health. In: *The Routledge International Handbook of Perinatal Mental Health Disorders.* London: Routledge; 2024. p. 53-71.
13. Roşian A, Zdrîncă M, Dobjanschi L, Vicaş LG, Mureşan ME, Dindelegan CM, et al. The role of vitamin D in the management of major depressive disorder: a systematic review. *Nutrients.* 2025;18(6):792.
14. Werner E, Le HN, Babineau V, Grubb M. Preventive interventions for perinatal mood and anxiety disorders: a review of selected programs. *Semin Perinatol.* 2024.
15. Bozzatello P, Novelli R, Montemagni C, Rocca P, Bellino S. Nutraceuticals in psychiatric disorders: a systematic review. *Int J Mol Sci.* 2024;25(9):4824.
16. Healy EH. Education on Omega-3 Fatty Acids to Improve Clinician Knowledge of Diet and Depression. Tucson: University of Arizona; 2023.
17. Høgh S, Hegaard HK, Renault KM, Cvetanovska E, Kjaerbye-Thygesen A, Juul A, et al. Short-term oestrogen as a strategy to prevent postpartum depression in high-risk women: protocol for the double-blind, randomised, placebo-controlled MAMA clinical trial. *BMJ Open.* 2021;11(12):e052922.

18. Sharma V, Sharkey KM, Palagini L, Mazmanian D, Thomson M. Preventing recurrence of postpartum depression by regulating sleep. *Expert Rev Neurother*. 2023;23(8):1-9.
19. Cattarinussi G, Segre G, Biaggi A, Hazelgrove K, Sambataro F, Russo M, et al. Neuropsychological performance in women at risk of postpartum depression and postpartum psychosis. *Arch Womens Ment Health*. 2025;28(1):55-65.
20. Gordon-Smith K, Ridley P, Perry A, Craddock N, Jones I, Jones L. Migraine associated with early onset postpartum depression in women with major depressive disorder. *Arch Womens Ment Health*. 2021;24(6):949-55.