

Integrative Lifestyle Medicine Approaches to Fibromyalgia and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Mini-Review

Sana Akhlaq¹, Uzma Aftab², Muhammad Abdullah Aftab Qureshi³, Farooq Azam Rathore⁴

Abstract

Chronic pain syndromes, such as fibromyalgia (FM) and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), represent a significant global health burden. Their etiology is complex and multifactorial, encompassing central sensitization, autonomic dysfunction, immune dysregulation, and mitochondrial abnormalities.

Lifestyle medicine emphasizes predominantly plant-based nutrition, physical activity, nocturnal restorative sleep, stress regulation, and social connectedness. It offers a structured evidence-based strategy for managing fibromyalgia and ME/CFS. First, anti-inflammatory, nutrient-dense diets modulate systemic inflammation, mitochondrial function, and neuroimmune activity. Then, graded exercise and mind-body practices alleviate widespread pain, persistent fatigue, and impaired functional capacity. Next, sleep optimization combined with cognitive-behavioural strategies effectively targets non-restorative sleep; and finally, peer support enhances social connectedness. Integrating these elements into individualized, multidisciplinary programmes, offers a holistic framework to address the core mechanisms of FM and ME/CFS while empowering patients to improve function and quality of life. This mini-review synthesizes contemporary evidence and identifies research and clinical opportunities, focusing on anti-inflammatory and antioxidant diets, neuro-nutritional approaches, nutraceuticals, the gut-brain axis, graded exercise therapy, mind-body practices, and cognitive-behavioural interventions.

Keywords: Fibromyalgia, ME/CFS, chronic fatigue syndrome, lifestyle medicine, plant-based diet, gut-brain axis.

DOI: <https://doi.org/10.47391/JPMA.26-85>

Introduction

Fibromyalgia (FM) and myalgic encephalomyelitis/chronic

fatigue syndrome (ME/CFS) are heterogeneous, multisystem disorders that create a substantial burden on healthcare systems and economies worldwide. Global prevalence estimates range from 2–8%, with women affected 7–9 times more frequently than men. The incidence rises with age. In Asia, prevalence is approximately 1.7% with a female-to-male ratio of 3:1.¹ In Pakistan, hospital-based prevalence estimates include 33.3% among 750 general hospital-visiting patients,² 13.66% in pre-dialysis chronic kidney disease patients,³ and lower proportions (e.g., 2.8% within muscle disorder cases) in neurology outpatients.⁴

The etiology of these conditions is multifactorial, involving central and peripheral sensitization, psychosocial stressors, immune dysregulation, genetic variants, gut-brain axis perturbations, autonomic imbalance and mitochondrial dysfunction.⁵ However, this mini-review focusses on selected, interrelated pathways most amenable to lifestyle interventions.

Contemporary research has shifted from purely biological or psychological explanations toward a centralized, multisystem model of fibromyalgia and ME/CFS. This model recognizes the combined role of central sensitization, neuroimmune activation, mitochondrial dysfunction, gut dysbiosis, and circadian rhythm disruption.⁶ Within this framework, neuro-nutrition, nutraceutical support, lifestyle medicine, and circadian entrainment may act together to influence symptom severity and disease course.

Neuro nutrition (also called neuronutrition) is the targetted use of specific nutrients, dietary components, bioactive molecules, and personalized nutrition strategies to support brain health, enhance resilience against stress and inflammation, and prevent or treat neurological disorders by modulating pathways like Nuclear factor erythroid 2-related factor 2 (Nrf2) signalling, epigenomics, and metabolomics.⁷ Circadian entrainment (the alignment of daily rhythms through timed light exposure, meals, and activity) supports modulation of the gut microbiota, immune function, and redox balance by synchronizing biological clocks.⁶ Personalized multimodal lifestyle intervention, defined as a tailored, evidence-based treatment approach for chronic pain that simultaneously addresses multiple modifiable lifestyle factors (such as

¹Gujranwala Medical College, Gujranwala Pakistan; ²Combined Military Hospital, Rawalpindi; ³Foundation University of Health Sciences, Islamabad, Pakistan; ⁴Quetta Institute of Medical Sciences (QIMS), Quetta, Pakistan.

Correspondence: Farooq Azam Rathore. e-mail: farooqrathore@gmail.com
ORCID ID: 0000-0002-4759-0453

physical activity/inactivity, stress management, sleep quality, nutrition/weight management, and related behavioural aspects in a customized way based on individual patient profiles, preferences, barriers, and shared decision-making, representing a paradigm shift from traditional tissue- or disease-focused care to holistic, biopsychosocial strategies that integrate motivational interviewing, pain neuroscience education, and stepped-care models to optimize outcomes and reduce pain persistence.⁸

Despite significant research, debate continues over whether pharmacological, non-pharmacological, or combined approaches are most effective. This mini review summarizes the evidence for personalized multimodal programmes based on the pillars of lifestyle medicine, augmented by insights into the gut-brain-immune axis and chronobiology. It examines how lifestyle-based interventions interact with neuroimmune, metabolic, and circadian mechanisms to influence symptom burden in fibromyalgia and ME/CFS.

Personalized Multimodal Integrated Lifestyle Interventions (PMLIs)

Individualized approach to every FM patient is important. PMLI refers to structured programmes that combine nutrition, physical activity, sleep optimization,

psychological therapies, and social support, tailored to individual symptom profiles and comorbidities. PMLIs an evidence-based approach that is better compared to single-modality treatments (Figure 1)

Nijs et al.⁸ documented that graded exercises yield standardized mean difference (SMD) 0.5–1.0 for pain reduction and function in fibromyalgia (20–40% improvement in RCTs); anti-inflammatory nutritional strategies (e.g., Mediterranean diets with vitamin D/B12/magnesium supplementation) achieve SMD –0.4 to –0.5 for pain intensity; cognitive behavioral therapy for insomnia (CBT-I) produces SMD –1.0 to –1.5 for sleep efficiency and SMD –0.8 for associated pain/fatigue (25–40% gains, sustained at 1 year); stress management via mindfulness or acceptance and commitment therapy (ACT) confers SMD 0.3–0.7 for catastrophizing and functional status (15–25% improvements). Integrated PMLIs in multidisciplinary settings result in 30–50% overall symptom reduction, enhanced adherence, and cost-effectiveness.⁸

1. Nutrition

Nutritional strategies target neuroimmune, mitochondrial, and gut-brain pathways implicated in FM and ME/CFS. Plant-predominant and Mediterranean-style patterns generally show more consistent benefits than highly

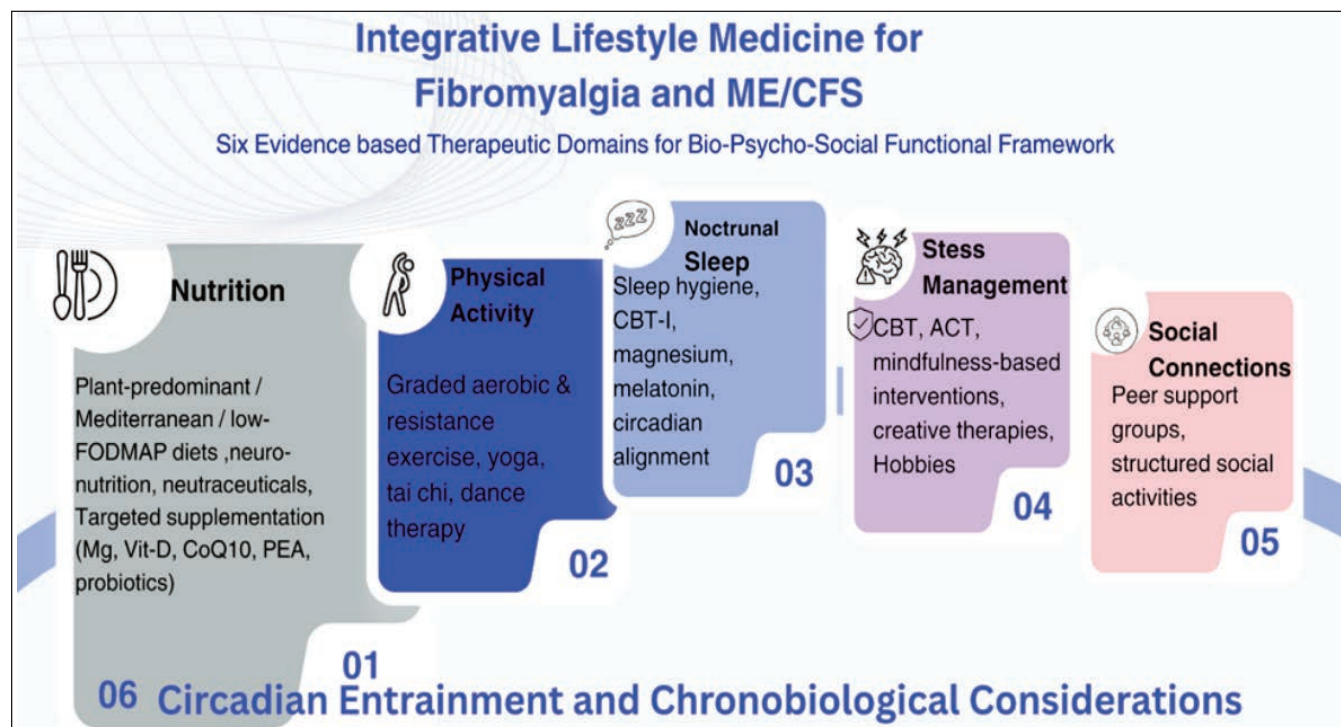


Figure: Integrative Lifestyle Medicine Framework for Fibromyalgia and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS).

FODMAP for Fermentable Oligo-, Di-, Mono-saccharides And Polyols), Mg for Magnesium, Vit-D for Vitamin D, CoQ10 for Coenzyme Q10, PEA for PEA = Palmitoylethanolamide, CBT for cognitive behavioral therapy, ACT for acceptance and commitment.

restrictive elimination diets.⁵

1.1 Neuro-nutrition

Neuro-nutrition refers to nutritional strategies that target nervous system function, including reduction of neuroinflammation, support for mitochondrial health, and modulation of central sensitization through diet and targeted nutrients. Plant-based diets rich in phytosterols and fibre attenuate symptoms in select cohorts via gut microbiome modulation and anti-inflammatory mechanisms.⁵ Low-FODMAP diets show particular promise for FM patients with overlapping functional gastrointestinal disorders, with early evidence of global symptom and quality-of-life improvement. Gluten-free diets may benefit non-celiac wheat-sensitive individuals by lowering pro-inflammatory cytokines.⁵

1.2 Nutraceuticals

Nutraceuticals are naturally derived compounds used in therapeutic doses to support physiological functions and reduce disease-related symptoms. In fibromyalgia and ME/CFS, nutraceuticals mainly target oxidative stress, neuroinflammation, mitochondrial dysfunction, and abnormal pain signalling via pathways such as p38-Mitogen-activated protein kinases, Nuclear factor kappa-light-chain-enhancer of activated B cells, COX-2, and pro-inflammatory cytokines (IL-1 β , IL-6, TNF- α).⁹

Agents such as palmitoylethanolamide (PEA), alpha-lipoic acid, curcumin, omega-3 fatty acids, coenzyme Q10, magnesium, and selected herbal compounds may reduce inflammatory signaling, calm microglial activation, and improve fatigue and pain.⁹

1.3 Vitamins

Low serum B12 and folate are frequently observed in FM patients and correlate with fatigue and neurological symptoms. Antioxidant vitamins (C, E, A) can counteract reduced endogenous defenses and lipid peroxidation. Vitamin D deficiency is common, especially in postmenopausal women, with studies showing significantly lower levels compared to controls, including in Pakistan.⁹

1.4 Minerals

Magnesium deficiency impairs ATP synthesis, exacerbates central sensitization via N-methyl-D-aspartate, receptor activation, and contributes to muscle spasms and inflammation. Iron deficiency anaemia is associated with increased incidence of FM, with ferric carboxymaltose significantly improving symptom severity in iron-deficient patients. Dietary polyphenols, despite extensive metabolism, exhibit anti-inflammatory and neuroprotective potential through modulation of NF- κ B

and Nrf2 pathways.⁹

1.5 Microbiome & Probiotics

Microbiota-modulating interventions (probiotics, prebiotics, faecal microbiota transplantation) are primarily useful in alleviating cognitive problems ("fibro fog") and mood disorders. Multi-strain probiotics reduce pain scores by 15–20% vs. placebo in FM patients, with improvements in memory/concentration.¹⁰ Prebiotics lower hs-CRP and improve psychological symptoms in metabolic syndrome. Increased short-chain fatty acid (SCFA)-producing bacteria (e.g., Bifidobacterium) are associated with better well-being and anti-inflammatory benefits. Rifaximin has been shown to modulate brain responses to stress and enhance mindfulness. Pilot studies suggest that faecal microbiota transplantation may reduce nociplastic pain and fatigue by 20–35%, although these findings remain preliminary and require confirmation in larger controlled trials. Probiotics improve cognition/mood (anxiety $\downarrow$ 15–25%, attention $\uparrow$ 10–20%) while nutritional approaches (e.g., Mediterranean diet) alleviate symptoms via SCFA restoration.¹¹ Probiotic modulation of the gut-brain axis re-establishes short-chain fatty acid production, subsiding FM's cognitive 'fibro-fog' and mood comorbidities.⁵

2. Physical Activity

Regular physical activity—whether graded aerobic exercise, resistance training, yoga, tai chi, aquatic therapy, or dance—consistently reduces pain and improves function in fibromyalgia. A 2022 systematic review of 20 studies (n=1,078) noted that 74% of interventions gave statistically significant pain reductions on quantitative scales, while fibromyalgia-specific trials narrated moderate improvements in tender-point counts and fatigue, with Fibromyalgia Impact Questionnaire (FIQ) scores decreasing 15–22%.¹²

3. Stress Management within Biopsychosocial Framework

Chronic stress and impaired emotional regulation are central amplifiers of fibromyalgia symptomatology. Women with fibromyalgia display distinctly elevated psychological distress ($p < 0.001$), higher life-event stress, perceived stress, and autonomic dysregulation (32% reduction in parasympathetic tone and 45% increase in LF/HF ratio). Cognitive-behavioural therapy (CBT) and acceptance and commitment therapy (ACT) yield moderate-to-large reductions in depression (SMD -0.72 , 95% CI -1.05 to -0.39) and anxiety (SMD -0.58 , 95% CI -0.89 to -0.27). Integrating structured psychological interventions is therefore crucial to break the vicious cycle of stress-induced nociceptive amplification.^{13,14}

4. Optimizing Nocturnal Sleep

Sleep disturbance and fibromyalgia are closely interrelated, with non-restorative sleep present in >90% of patients and serving as both consequence and perpetuator of central sensitization. Cognitive behavioural therapy for insomnia (CBT-I) produces robust, clinically meaningful improvements in sleep quality (SMD -0.63 , 95% CI -0.98 to -0.27), outperforming most pharmacological sleep agents in sustainability and safety. Adjunctive strategies—including magnesium and melatonin supplementation, regular physical activity, and circadian alignment—further enhance sleep architecture and daytime functioning, making it a non-negotiable therapeutic target.^{15,16}

5. Positive Social Connections

Perceived social support acts as a powerful buffer against the psychological and functional impairment in fibromyalgia. In a cohort of 200 affected individuals, pain intensity strongly predicted emotional dysregulation ($r=0.52$, $p<0.001$), which in turn worsened depression, anxiety, disability, and quality of life. Higher social support significantly modulates these pathways ($p=0.002$), reducing depressive symptoms by 15–20%. Structured peer-support programmes and facilitated group activities should therefore be routinely incorporated into their plans.¹⁷

6. Circadian Entrainment and Chronobiological Considerations

Circadian entrainment refers to the synchronization of the body's internal biological clock with external time cues such as light exposure, meal timing, physical activity, and sleep–wake schedules. Non-responders to serotonin–noradrenaline reuptake inhibitors manifest pronounced evening chronotype, greater rhythm disruption ($p<0.001$), delayed sleep–wake patterns, and poorer sleep quality ($p=0.002$). Simple entrainment strategies—including consistent sleep timing, morning light exposure, regular meal schedules, timed physical activity, and judicious use of melatonin—help restore circadian stability.¹⁸

Evidence Gaps and Future Directions

Despite promising findings, several limitations warrant caution. Many studies are small, heterogeneous, or preliminary, and larger, well-powered randomized controlled trials (RCTs) are needed. Head-to-head comparisons with standard pharmacotherapy remain scarce. There is also underrepresentation of diverse populations, including those from South Asia and low-resource settings such as Pakistan, where cultural, socioeconomic, and healthcare access factors may influence outcomes.

Conclusions

While pharmacological options remain useful for symptom control in selected patients, the most consistent and clinically meaningful improvements in pain, fatigue, sleep, mood, and quality of life appear to arise from integrated lifestyle and neuro-nutritional interventions. These approaches are generally safe, cost-effective, and empowering, shifting patients from passive recipients to active participants in their care.

AI use Disclosure: After completing the final draft, Dr Rathore used ChatGPT V 5.2 – OpenAI (19th Jan 2026) to improve the language, grammar and syntax of the manuscript without any significant changes in the actual text.

References

1. Tahir S, Zeb A, Sharif M, ur Rehman O, Khan MS, Mukhtar M et al. The prevalence of fibromyalgia among doctors in the tertiary care hospital: A cross-sectional study. *Ann Med Surg (Lond)*. 2022; 2022 1;84:104931. doi: 10.1016/j.jamsu.2022.104931
2. Arif MA, Syed F, Niazi R, Arif SA, Hashmi UEL, Shah Z. The oracle study - fibromyalgia, prevalence and severity in the hospital setting in the Pakistani population. *J Pak Med Assoc*. 2021;71:1357-1368. doi:10.47391/JPMA.1000
3. Khan Z, Naqvi R. Prevalence of Fibromyalgia in chronic kidney disease pre-dialysis patients: Experience from a Tertiary Care Renal unit in Pakistan. *Pak J Med Sci*. 2021;37:1939-1942. doi:10.12669/pjms.37.7.4474
4. Awan S, Siddiqi AI, Asif A, Ahmed N, Brohi H, Jalbani S, Wasay M. Spectrum of neurological disorders in neurology outpatients clinics in urban and rural Sindh, Pakistan: a cross sectional study. *BMC Neurol*. 2019;19:192. doi:10.1186/s12883-019-1424-1
5. Badaeva A, Danilov A, Kosareva A, Lepshina M, Novikov V, Vorobyeva Y, et al. Neuronutritional approach to fibromyalgia management: a narrative review. *Pain Ther*. 2024;13:1047-61. doi: 10.1007/s40122-024-00641-2.
6. Carrasco-Querol N, Cabricano-Canga L, Bueno Hernández N, Gonçalves AQ, Caballol Angelats R, Pozo Ariza M, et al. Nutrition and Chronobiology as Key Components of Multidisciplinary Therapeutic Interventions for Fibromyalgia and Associated Chronic Fatigue Syndrome: A Narrative and Critical Review. *Nutrients*. 2024;16:182. doi: 10.3390/nu16020182
7. Scuto MC, Anfuso CD, Lombardo C, Di Fatta E, Ferri R, Musso N et al. Neuronutrition and Nrf2 Brain Resilience Signaling: Epigenomics and Metabolomics for Personalized Medicine in Nervous System Disorders from Bench to Clinic. *Int J Mol Sci*. 2025 ;26:9391. doi: 10.3390/ijms26199391.
8. Nijs J, Malfliet A, Roose E, Lahousse A, Van Bogaert W, Johansson E, et al. Personalized multimodal lifestyle intervention as the best-evidenced treatment for chronic pain: state-of-the-art clinical perspective. *J Clin Med*. 2024;13:644. doi: 10.3390/jcm13030644.
9. Antonelli A, Bianchi M, Fear EJ, Giorgi L, Rossi L. Management of Fibromyalgia: Novel Nutraceutical Therapies Beyond Traditional Pharmaceuticals. *Nutrients*. 2025;17:530. doi: 10.3390/nu17030530.
10. Dipalma G, Marinelli G, Ferrante L, Di Noia A, Carone C, Colonna V, et al. Modulating the Gut Microbiota to Target Neuroinflammation, Cognition and Mood: A Systematic Review of Human Studies with Relevance to Fibromyalgia. *Nutrients*. 2025;17:2261. doi: 10.3390/nu17142261

11. Watai K, Taniguchi M, Azuma K. The Gut–Brain–Immune Axis in Environmental Sensitivity Illnesses: Microbiome-Centered Narrative Review of Fibromyalgia Syndrome, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, and Multiple Chemical Sensitivity. *Int J Mol Sci.* 2025 ;26:9997. doi: 10.3390/ijms 26209997.
12. Hickman B, Pourkazemi F, Pebdani RN, Hiller CE, Fong Yan A. Dance for chronic pain conditions: a systematic review. *Pain Med.* 2022;23:2022-41. doi: 10.1093/pm/pnac092.
13. Lledó Boyer A, López-Roig S, Pastor-Mira MÁ, Terol Cantero MC, Martín-Aragón M. Exploring Biopsychosocial Stress Markers in Women With Fibromyalgia. *Pain Manag Nurs* 2024;25:e336-e45. doi: 10.1016/j.pmn.2024.05.008.
14. Cojocaru CM, Popa CO, Schenk A, Suciú BA, Szasz S. Cognitive-behavioral therapy and acceptance and commitment therapy for anxiety and depression in patients with fibromyalgia: A systematic review and meta-analysis. *Med Pharm Rep.* 2024;97:26. doi: 10.15386/mpr-2661.
15. Pathak A, Kelleher EM, Brennan I, Amarnani R, Wall A, Murphy R, et al. Treatments for enhancing sleep quality in fibromyalgia: a systematic review and meta-analysis. *Rheumatology (Oxford).* 2025;64:4495-4516. doi: 10.1093/rheumatology/keaf147.
16. Hudson J, Imamura M, Robertson C, Whibley D, Aucott L, Gillies K, et al. Effects of Pharmacologic and Nonpharmacologic Interventions for the Management of Sleep Problems in People With Fibromyalgia: Systematic Review and Network Meta-Analysis of Randomized Controlled Trials. *Arthritis Care Res (Hoboken).* 2025 ;77:1095-1105. doi: 10.1002/acr.25505.
17. Telli H, Akkus M. The interplay of pain, emotional regulation difficulties, and social support in individuals diagnosed with fibromyalgia: impact on depression, anxiety, functional disability, and quality of life. *Psychol Health Med.* 2025;30:1540-59. doi: 10.1080/13548506.2025.2469191.
18. Krupa AJ, Chrobak AA, Sołtys Z, Korkosz M, Nowakowski J, Dudek D, et al. Chronobiological variables predict non-response to serotonin and noradrenaline reuptake inhibitors in fibromyalgia: a cross-sectional study. *Rheumatol Int.* 2024;44:1987-95. doi: 10.1007/s00296-024-05650-0