Commentary

Discovery Medicine 2026; 38(206): 972–974
https://doi.org/10.24976/Discov.Med.202638206.78

A Pragmatic Approach to Laboratory Testing in Fibromyalgia: Revisiting the Essentials

Jozélio Freire de Carvalho[1,*]

[1]Instituto de Ciências da Saúde, Universidade Federal da Bahia, 40170-110 Salvador, BA, Brazil
*Correspondence: jotafc@gmail.com (Jozélio Freire de Carvalho)
Submitted: 28 November 2025 Accepted: 2 February 2026 Published: 20 March 2026

Introduction

Fibromyalgia (FM) is a clinical diagnosis characterized by widespread musculoskeletal pain, fatigue, and sleep disturbance. Nevertheless, diagnostic evaluation is frequently excessive, reflecting the persistent misconception that FM must be established as a diagnosis of exclusion. Such overtesting contributes to increased healthcare costs, low-value care, and may result in false-positive findings that ultimately misdirect clinical management [1–3].

Recent international and national guidelines consistently emphasize that FM should be approached as a positive clinical diagnosis, grounded in characteristic symptom patterns rather than extensive exclusionary testing. Recommendations from the Royal College of Physicians (United Kingdom) [1], the American Academy of Family Physicians [3], the European League Against Rheumatism (EULAR) [4], the American College of Rheumatology (ACR) [5], the Sociedade Brasileira de Reumatologia [6], the Israeli Rheumatology Association [7], and the Portuguese Direção-Geral da Saúde [8] converge in advocating that laboratory investigation be concise, targeted, and driven by clinical hypotheses.

Collectively, these documents agree that a limited baseline laboratory panel is generally sufficient to exclude common alternative diagnoses and relevant comorbidities, as summarized in Tables 1,2. This commentary integrates these recommendations—placing particular emphasis on the Portuguese DGS Norm 017/2016—to propose a pragmatic, cost-effective, and evidence-aligned approach to laboratory testing in patients with suspected fibromyalgia.

Evidence From Guidelines

The RCP (2022) recommends a compact laboratory panel comprising complete blood count (CBC), erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), creatine kinase (CK), thyroid-stimulating hormone (TSH), glucose, renal function tests (urea and creatinine), and liver function tests [1]. These investigations address common differential diagnoses, including hypothyroidism, inflammatory myopathies, diabetes mellitus, and hepatic or renal disease, as summarized in Table 1.

The Canadian guidelines and the American Academy of Family Physicians (AAFP) recommendations similarly restrict routine testing to CBC, ESR/CRP, CK, and TSH, unless clinical suspicion clearly indicates otherwise [2,3].

The EULAR and ACR documents emphasize that fibromyalgia is a positive clinical diagnosis, based on characteristic symptom patterns rather than a diagnosis of exclusion, and explicitly discourage extensive laboratory testing in the absence of clinical red flags [4,5].

In Brazil, the Sociedade Brasileira de Reumatologia (SBR) reiterates that ESR and CRP are usually normal in FM and that additional investigations should be guided by differential diagnostic suspicion [6], a position that remains consistent with the most recent Brazilian Society of Rheumatology consensus documents on fibromyalgia management published in 2026, which reinforce a pragmatic and patient-centered approach aligned with international recommendations [9,10].

In Israel, the Israeli Rheumatology Association (IRA) consensus (Harefuah 2013) aligns with this approach, advocating selective use of laboratory testing guided by clinical findings [7].

In Portugal, the DGS Norm 017/2016 (updated in 2017) recommends a similar minimalist panel—CBC, ESR/CRP, TSH, CK, hepatic and renal function tests, and glucose—highlighting that these investigations are sufficient to rule out frequent mimickers such as hypothyroidism, myopathies, and metabolic bone disease [8].

When to Broaden the Investigation

Further testing should be guided by clinical cues: objective arthritis or systemic features → autoimmune serology; focal weakness or markedly elevated CK → evaluation for myositis or drug-induced myopathy; persistent fatigue with abnormal liver enzymes or elevated alkaline phosphatase (ALP) → assessment for hepatic disease or osteomalacia; weight loss, fever, or anemia → malignancy or infection screening; and excessive daytime somnolence → sleep study.

The Portuguese DGS guideline also notes that calcium, phosphorus, and vitamin D levels may be assessed

Table 1. Recommended laboratory tests in fibromyalgia.

Recommended tests	Purpose/differential diagnosis	Comments
Complete blood count (CBC)	Detect anemia, infection, cytopenia	
ESR or CRP	Screen for systemic inflammation	
Creatine kinase (CK)	Identify muscle disease or statin-induced myopathy	
Thyroid-stimulating hormone (TSH)	Exclude hypothyroidism	Common mimicker of FM
Glucose or HbA1c	Detect metabolic causes of fatigue	Diabetes/metabolic syndrome
Urea and creatinine	Evaluate renal/metabolic profile	Rule out other causes of fatigue
Liver function tests (AST, ALT, γ-GT, ALP)	Detect hepatic disease; ALP also assists in excluding osteomalacia	Osteomalacia is a key treatable differential diagnosis for diffuse pain

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CBC, complete blood count; CK, creatine kinase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FM, fibromyalgia; HbA1c, glycated hemoglobin; γ-GT, gamma-glutamyl transferase; TSH, thyroid-stimulating hormone.

Table 2. Tests not routinely recommended in fibromyalgia.

Not routinely indicated	Reason/note
ANA, RF, anti-CCP, ENA panel	High false-positive rate; order only with autoimmune features
Vitamin D	Test only in high-risk or symptomatic deficiency
Vitamin B12	Consider only in dietary restriction or neuropathic symptoms
Extensive imaging (MRI, CT)	No role in typical FM presentation
FM/a® or “biomarker” assays	Commercial immunologic fibromyalgia test; not validated by guidelines

Abbreviations: ANA, antinuclear antibodies; anti-CCP, anti-cyclic citrullinated peptide; ENA, extractable nuclear antigens; FM/a®, fibromyalgia assay; MRI, magnetic resonance imaging; RF, rheumatoid factor; CT, computed tomography.

when bone or metabolic pathology is suspected, aligning with the rationale to exclude osteomalacia or hypovitaminosis D [8].

Clinical and Economic Rationale

Excessive laboratory testing contributes to diagnostic delay, patient anxiety, and unnecessary healthcare costs, whereas a rational baseline panel helps ensure diagnostic clarity. Observational studies indicate that up to 40% of patients with FM undergo autoimmune serology or imaging investigations without meaningful diagnostic yield [9–13]. Integrating international and Portuguese recommendations into a unified, evidence-based protocol improves cost-effectiveness and reduces medicalization (see Tables 1 and 2)[14].

Misdiagnosis and overdiagnosis remain important challenges in the clinical assessment of patients with fibromyalgia, particularly when the condition is approached primarily through extensive exclusionary testing. Evidence indicates that indiscriminate diagnostic strategies may lead to unnecessary investigations, delayed diagnosis, and inappropriate labeling, ultimately contributing to patient anxiety and increased healthcare utilization. Adopting a positive, symptom-based diagnostic framework—supported by targeted laboratory evaluation—helps mitigate these risks and aligns clinical practice with contemporary recommendations [15].

Osteomalacia remains a key, treatable differential diagnosis for diffuse musculoskeletal pain, particularly in the presence of elevated alkaline phosphatase (ALP); therefore, its exclusion is essential before confirming a diagnosis of FM [8].

Conclusion

A pragmatic laboratory approach to fibromyalgia should prioritize precision over proliferation. In most cases, a single baseline panel—comprising CBC, ESR or CRP, CK, TSH, glucose, and renal and hepatic profiles—is sufficient. Among hepatic parameters, alkaline phosphatase (ALP) plays a dual role in identifying hepatic dysfunction and excluding osteomalacia. The Portuguese DGS Norm 017/2016 reinforces this principle, noting that calcium, phosphorus, or vitamin D testing should be considered only when there is clinical suspicion of bone or metabolic disease.

Expansion beyond this minimal set should rely exclusively on specific clinical findings. This unified, guideline-driven approach streamlines care, minimizes false-positive results, prevents overdiagnosis, and supports appropriate management focused on patient education and long-term outcomes.

Availability of Data and Materials

All data analyzed during this study are included in this published article.

Author Contributions

JFdC conceived the study, performed the literature review, analyzed and interpreted the data, and drafted and critically revised the manuscript. The author approved the final version of the manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

The author thanks the national and international rheumatology societies whose clinical guidelines and consensus documents informed this work.

Artificial intelligence–assisted language editing was performed using ChatGPT (OpenAI, GPT-5.2 model). No content generation, data analysis, or reference creation was conducted using AI tools. The author retains full responsibility for the manuscript.

Funding

This research received no external funding.

Conflict of Interest

Jozélio Freire de Carvalho is serving as one of the Editorial Board members of this journal. We declare that Jozélio Freire de Carvalho had no involvement in the review of this article and has no access to information regarding its review.

References

[1] Royal College of Physicians. The Diagnosis of Fibromyalgia Syndrome. RCP: London. 2022.

[2] Fitzcharles MA, Ste-Marie PA, Goldenberg DL, Pereira JX, Abbey S, Choinière M, *et al*. 2012 Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome: executive summary. Pain Research & Management. 2013; 18: 119–126. https://doi.org/10.1155/2013/918216.

[3] Winslow BT, Vandal C, Dang L. Fibromyalgia: Diagnosis and Management. American Family Physician. 2023; 107: 137–144.

[4] Macfarlane GJ, Kronisch C, Dean LE, Atzeni F, Häuser W, Fluß E, *et al*. EULAR revised recommendations for the management of fibromyalgia. Annals of the Rheumatic Diseases. 2017; 76: 318–328. https://doi.org/10.1136/annrheumdis-2016-209724.

[5] Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RL, *et al*. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Seminars in Arthritis and Rheumatism. 2016; 46: 319–329. https://doi.org/10.1016/j.semarthrit.2016.08.012.

[6] Heymann RE, Paiva ES, Martinez JE, Helfenstein M, Jr, Rezende MC, Provenza JR, *et al*. New guidelines for the diagnosis of fibromyalgia. Revista Brasileira De Reumatologia. 2017; 57 Suppl 2: 467–476. https://doi.org/10.1016/j.rbre.2017.07.002.

[7] Ablin JN, Amital H, Ehrenfeld M, Aloush V, Elkayam O, Langevitz P, *et al*. Guidelines for the diagnosis and treatment of the fibromyalgia syndrome. Harefuah. 2013; 152: 742–747, 751, 750. (In Hebrew)

[8] Direção-Geral da Saúde (Portugal). Norma n.º 017/2016 – Abordagem Diagnóstica da Fibromialgia (Atualização 2017). Ministério da Saúde: Lisboa. 2017. Available at: https://www.aped-dor.org/documentos/DGS-AbordagemDiagnosticaFibromialgia-2017.pdf (Accessed: 12 March 2026).

[9] Heymann RE, Rezende MC, Braz ADS, Ranzolin A, Reis APMG, Golmia APF, *et al*. Brazilian Society of Rheumatology's fibromyalgia treatment guidelines - part I: monitoring and non-pharmacological management. Advances in Rheumatology (London, England). 2026; 66: 10. https://doi.org/10.1186/s42358-025-00507-x.

[10] Heymann RE, Rezende MC, Paiva EDS, de Assis MR, de Sousa Braz A, Ranzolin A, *et al*. Review of fibromyalgia treatment guidelines: part 2 - pharmacological treatment. Advances in Rheumatology (London, England). 2026; 66: 9. https://doi.org/10.1186/s42358-025-00483-2.

[11] Häuser W, Wolfe F. Diagnosis and diagnostic tests for fibromyalgia (syndrome). Reumatismo. 2012; 64: 194–205. https://doi.org/10.4081/reumatismo.2012.194.

[12] Verkerk EW, Tanke MAC, Kool RB, van Dulmen SA, Westert GP. Limit, lean or listen? A typology of low-value care that gives direction in de-implementation. International Journal for Quality in Health Care: Journal of the International Society for Quality in Health Care. 2018; 30: 736–739. https://doi.org/10.1093/intqhc/mzy100.

[13] Mafi JN, Parchman M. Low-value care: an intractable global problem with no quick fix. BMJ Quality & Safety. 2018; 27: 333–336. https://doi.org/10.1136/bmjqs-2017-007477.

[14] Jones EA, Asaad F, Patel N, Jain E, Abd-Elsayed A. Management of Fibromyalgia: An Update. Biomedicines. 2024; 12: 1266. https://doi.org/10.3390/biomedicines12061266.

[15] Di Carlo M, Bianchi B, Salaffi F, Pellegrino G, Iannuccelli C, Giorgi V, *et al*. Fibromyalgia: one year in review 2024. Clinical and Experimental Rheumatology. 2024; 42: 1141–1149. https://doi.org/10.55563/clinexprheumatol/mbyi1n.