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Opinion Article

Biomarker Panels in Early Detection of Multiple Sclerosis: A Meta-Analytical Review

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DESCRIPTION

Multiple Sclerosis (MS), a chronic demyelinating disorder of the central nervous system, is notoriously difficult to diagnose in its earliest stages. Clinicians are often challenged by the variable presentation of symptoms and the lack of a definitive diagnostic test. Despite advances in imaging and immunology, the average time from symptom onset to formal diagnosis can still span months, if not years. Early detection, however, is critical especially given the mounting evidence that Disease-Modifying Therapies (DMTs) are most effective when initiated at the earliest clinical or radiographic signs of disease.

This diagnostic gap has spurred a growing interest in biomarker panels combinations of biological indicators that, when evaluated together, could offer higher sensitivity and specificity than single markers. Over the past decade, a wealth of studies has emerged exploring the utility of various biomarkers, including immunological, proteomic, genomic and metabolomics signatures, in identifying individuals at high risk of developing MS or in the early stages of the disease. A recent wave of meta-analyses has attempted to distil these findings into more actionable clinical understanding. Based on the evidence from these reviews, it is becoming increasingly clear that no single biomarker provides sufficient diagnostic accuracy to stand alone. However, composite biomarker panels, incorporating multiple parameters across different biological systems, are showing significant promise. For example, a panel combining Neurofilament Light Chain (NfL), Glial Fibrillary Acidic Protein (GFAP) and Oligo Clonal Bands (OCBs) in Cerebrospinal Fluid (CSF) has demonstrated predictive value for conversion from Clinically Isolated Syndrome (CIS) to relapsing-remitting MS (RRMS) in several high-quality studies.

Other promising candidates include chitinase-3-like protein 1 (CHI3L1), interleukin-6 (IL-6) and CXCL13, all of which have been linked to neuroinflammation and disease progression. Meta-analytical data suggest that when used in combination, these biomarkers improve diagnostic sensitivity by up to 30% compared to conventional clinical criteria alone. In addition, blood-based biomarkers, including serum NfL and microRNAs, offer a less invasive alternative to CSF sampling, making them more suitable for screening or routine monitoring. Despite these advances, the field faces several hurdles before biomarker panels can be adopted into everyday clinical practice. One major issue is heterogeneity in study design and methodology across the included trials. Differences in sample handling, assay platforms, patient cohorts and endpoint definitions make it difficult to synthesize findings with high confidence. Many meta-analyses report moderate-to-high statistical heterogeneity, which undermines the generalizability of the pooled results. Another barrier is standardization and validation. While several biomarkers have shown reproducible results in research settings, few have undergone large-scale validation in independent, prospective cohorts. Regulatory approval processes also lag behind, partly because biomarker panel development requires consensus not just on individual markers, but on combinations, thresholds and interpretation algorithms.

Furthermore, economic and logistical considerations must not be ignored. Multi-analyte testing is resource-intensive, particularly when relying on CSF-based markers or advanced molecular platforms. High-income countries may be well-positioned to absorb these costs in tertiary care centers, but scalability across primary care or in low-resource settings remains a challenge. Nonetheless, the trajectory of biomarker research in MS is encouraging. The integration of biomarker panels with clinical data, MRI findings and genetic risk scores may soon allow clinicians to move from a reactive to a predictive model of care. Machine learning approaches are already being tested to interpret complex biomarker signatures and stratify patients into risk categories. This personalized approach could help identify individuals at highest risk for progression, allowing earlier and more targeted interventions.

CONCLUSION

The emerging consensus from meta-analytical studies is clear: biomarker panels hold substantial promise in improving the early detection of multiple sclerosis. While no single marker has proven sufficient, combinations of immunological, inflammatory and neurodegenerative indicators are beginning to

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provide a clearer diagnostic picture especially when used alongside clinical and imaging data. Despite methodological and logistical challenges, continued refinement of these panels and broader validation efforts are well underway. With advancements in multiplex assay technologies, computational analysis and international collaboration, the integration of biomarker panels into clinical neurology is within reach. Early detection is the key to altering the course of MS. The tools are emerging what remains is the collective effort to validate, standardize and implement them effectively. Biomarker panels, if thoughtfully developed and applied, could become a cornerstone of precision neurology, transforming how we diagnose and manage multiple sclerosis in the years ahead.