A blood test shows MS worsening one to two years before it happens

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Multiple sclerosis patients whose blood tests reveal elevated NfL, a biomarker of nerve damage, could see worsening disability one to two years later, according to a new study spearheaded by researchers at UC

San Francisco.

The study is the first to quantify the timeframe preceding disability worsening in which injury to the central nervous system takes place, said co-first author Ahmed Abdelhak, MD, of the UCSF Department of Neurology and the Weill Institute for Neurosciences.

Almost 1 million Americans suffer from MS. In advanced cases, patients may have limited mobility and experience spasticity, weakness, poor coordination and incontinence. However, recent advances suggest that more severe symptoms can be substantially delayed or even averted.

"This rising of NfL up to two years before signs of disability worsening, represents the window when interventions may prevent worsening," said Abdelhak.

In the study, published in *JAMA Neurology* on Nov. 6, 2023, and co-led by University Hospital and University of Basel, in Switzerland, the researchers looked at the incidence of disability worsening, defined as six months or more of increased impairment reflected in a higher score on the Expanded Disability Status Scale. They distinguished between disability worsening with relapse, which involves residual symptoms or the return of old ones following relapse, and gradual progression of symptoms without relapse.

91% at elevated risk of developing disability worsening

The researchers tracked data spanning a 10-year period from approximately 4,000 patient visits to UCSF, comprising the EPIC study, and from approximately 9,000 patient visits to multiple sites in Switzerland, comprising the SMSC study. Together, the two studies

included almost 1,900 patients. Among those, 570 patients were identified with disability that continued to worsen, of which the majority were independent of relapses.

Elevated NfL levels were associated with up to a 91% higher risk of worsening disability with relapse approximately a year later, and up to a 49% higher risk of worsening disability without relapse nearly two years later, the researchers found.

"We think that NfL elevation occurs earlier in disability worsening without relapse," said Abdelhak. This different pattern may indicate "a more prolonged process that decreases in intensity in advance of increased impairment," said co-senior author Ari Green, MD, medical director of the UCSF Multiple Sclerosis and Neuroinflammation Center.

"This aligns with recognition that death of nerve cells is a slow process that builds toward permanent disability and means that interventions to protect nerve cells might have time to also stop disability," he said.

"In addition to the groundbreaking findings on the temporal relationship between NfL increases and gradual disease progression in MS, the study supports the important role of NfL as an early marker of nerve damage," said co-senior author Jens Kuhle, MD, Ph.D., who led the Swiss cohort and is head of the Multiple Sclerosis Center at University Hospital and University of Basel, Switzerland. "Monitoring NfL levels might be able to detect disease activity with higher sensitivity than clinical exam or conventional imaging," he said.

Future investigation will look into therapies that can stop progression during this period of elevated NfL.

More information: Ahmed Abdelhak et al, Neurofilament Light Chain Elevation and Disability Progression in Multiple Sclerosis, *JAMA*

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