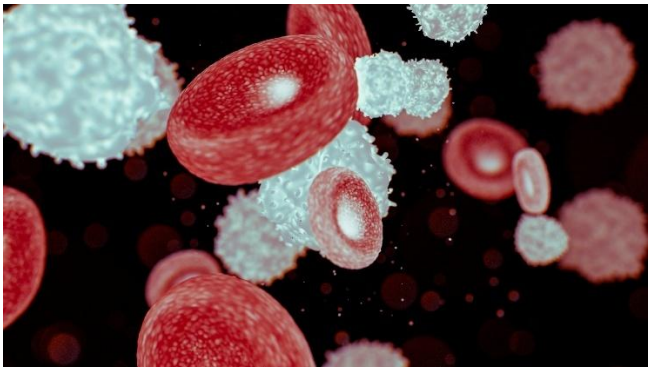
Why Chronic Diseases Cluster as we Age Explained by Common Blood Signals

Researchers identified shared and pattern-specific blood biomarkers that track multimorbidity and the rate of disease accumulation using population-based cohorts and modern statistical learning methods.



Study

This prospective observational analysis used data from the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K), which enrolled community-dwelling adults aged 60 years or older. Of the 3,363 participants at baseline, 2,247 had complete serum biomarker data and were followed for up to 15 years.

Clinicians recorded information on 60 categories of chronic diseases using interviews, physical examinations, laboratory testing, medication records, and registry linkage. Diagnoses were coded using the ICD-10. Functional and cognitive status were assessed using activities of daily living (ADL) measures and the Mini-Mental State Examination (MMSE).

Blood biomarkers were quantified using multiplex Luminex and single-molecule array (Simoa) platforms, along with accredited clinical assays for hemoglobin, albumin, and gamma-glutamyl transferase (GGT). This approach distinguished routinely available clinical markers from research-grade multiplex measurements.

To identify multimorbidity patterns and their biological correlates, the researchers applied the Least Absolute Shrinkage and Selection Operator (LASSO) regression in cross-sectional analyses. Linear mixed-effects models estimated individual rates of disease accumulation over time, defined as the average increase in chronic conditions per year and reflecting population-level trends rather than individual prediction.

Gaussian LASSO regression identified biomarkers associated with faster disease accumulation, while principal component analysis (PCA) summarized correlated biomarker subprofiles. For external validation, LASSO coefficients derived from SNAC-K were applied to the Baltimore Longitudinal Study of Aging (BLSA) cohort.

Findings

Participants had a mean age of 72.7 years, and 61.5% were women. At baseline, individuals had an average of 3.9 chronic diseases and used 3.7 medications. Mean MMSE score was 28.3, and 4.3% reported at least one ADL limitation.

Latent class analysis identified five multimorbidity patterns among individuals with two or more diseases: Unspecific; Neuropsychiatric; Psychiatric and Respiratory; Sensory Impairment and Anemia; and Cardiometabolic, alongside a no-multimorbidity group. These patterns represent statistical groupings rather than discrete clinical diagnoses.

The Neuropsychiatric pattern was characterized by older age, greater disability, polypharmacy, and cognitive impairment. The Cardiometabolic pattern showed high cardiovascular risk and medication burden, while the Psychiatric and Respiratory pattern involved younger individuals with modest disability. The Sensory Impairment and Anemia pattern was associated with relatively mild functional impairment.

Across the cohort, higher chronic disease counts were associated with cystatin C, hemoglobin A1c (HbA1c), growth differentiation factor 15 (GDF15), leptin, insulin, neurofilament light chain (NfL), creatinine, and C-peptide, while hemoglobin showed an inverse association.

Multinomial analyses revealed shared associations across all multimorbidity patterns for C-peptide, creatinine, cystatin C, GDF15, folic acid, HbA1c, insulin, leptin, and total cholesterol. The amyloid-β 42/40 ratio and hemoglobin were inversely associated overall, although hemoglobin showed a positive association within the Unspecific pattern.

Stronger pattern-specific links were observed between GDF15 and the Neuropsychiatric and Cardiometabolic patterns, and between cystatin C and creatinine with the Cardiometabolic and Sensory Impairment and Anemia patterns.

Conclusion

This population-based study demonstrates that blood biomarkers capture both shared and pattern-specific biological features of multimorbidity. GDF15, HbA1c, cystatin C, leptin, and insulin were consistently associated with higher disease burden, while GGT and albumin were associated with faster or slower rates of disease accumulation.

Although PCA highlighted a recurring axis related to mitochondrial and renal stress, these findings are observational and do not establish causality. Overall, the results suggest that age-related metabolic and systemic stress reflects biological vulnerability common to multiple chronic diseases, rather than providing immediate or individualized clinical risk prediction tools.

Source:

https://www.news-medical.net/news/20260105/Common-blood-signals-explain-why-chronic-diseases-cluster-as-we-age.aspx