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Research Article

Early Alzheimer's Detection through Blood Testing: Relevance to Aging Populations in Low- and Middle-income Countries

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Abstract

Alzheimer's disease is a leading cause of dementia worldwide, with timely diagnosis remaining a challenge, especially in low- and middle-income countries (LMICs). Limited access to specialized services, high costs of neuroimaging and cerebrospinal fluid analyses, and low public awareness delay recognition and treatment. This underscores the need for accessible, affordable, and scalable tools to identify individuals at risk earlier in the disease course.

The Triglyceride-Glucose (TyG) index, derived from routine blood tests, has emerged as a promising candidate for such screening. Elevated TyG values have been linked with cognitive decline and Alzheimer's disease, positioning it as a simple and cost-effective predictor. Unlike advanced imaging or biomarker testing, TyG screening requires no specialized infrastructure and can be incorporated into existing diabetes and cardiovascular programs, making early detection feasible at virtually no additional cost.

While not a substitute for definitive diagnostics, the TyG index offers an attractive adjunct for early risk stratification in LMICs. Its integration into primary care could bridge diagnostic gaps, enable earlier intervention, and help reduce the growing burden of dementia in resource-limited settings.

More Information

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Low- and middle-income countries (LMICs), including Pakistan, face important challenges in dementia recognition and care because of limited public awareness, restricted access to specialist services, and gaps in diagnostic infrastructure. Published Pakistani studies and reviews describe a substantial burden of geriatric morbidity and important limitations in dementia care and research capacity [1–3]. These circumstances underscore the need for accessible, affordable, and scalable approaches that can identify people who may benefit from further cognitive assessment. However, population-level estimates vary considerably across studies, and the available evidence should not be interpreted as establishing a precise national prevalence of dementia.

Emerging evidence identifies the Triglyceride-Glucose (TyG) index, derived from fasting triglyceride and glucose concentrations, as a potential marker of metabolic risk associated with cognitive decline. The TyG index is commonly used as a surrogate measure of insulin resistance. Altered insulin signaling has been implicated in neuronal dysfunction, inflammation, oxidative stress, vascular injury, and pathways involving amyloid-beta and tau, providing biological plausibility for an association between metabolic dysfunction and neurodegeneration [4,5]. In a longitudinal cohort, higher TyG was associated with greater risk of cognitive decline [6]. A prospective cohort study subsequently reported an association between an intermediate TyG category and incident Alzheimer's disease, although the association was not statistically significant when TyG was analyzed continuously [7]. A 2023 meta-analysis of 10 studies found that higher TyG was associated with cognitive impairment and dementia, but the certainty of evidence ranged from very low to moderate depending on the outcome and analysis [8]. A 2024 systematic review and meta-analysis of 17 studies also reported higher TyG among people with cognitive decline, while emphasizing heterogeneity across studies [9]. The MIND-China study further reported associations between TyG, dementia, Alzheimer's disease, and plasma Alzheimer's-related biomarkers [10]. Col-

lectively, these findings support further evaluation of TyG as a risk-stratification marker, but they do not establish it as a diagnostic test for Alzheimer's disease.

Collectively, the available evidence suggests that the TyG index may have value as an economical metabolic risk marker in LMICs, particularly where advanced neuroimaging and CSF biomarker testing are difficult to access. Amyloid PET and CSF testing remain important tools for establishing Alzheimer's disease pathology, but their cost, infrastructure requirements, and need for specialized personnel can limit broad implementation in resource-constrained settings [11,12]. TyG testing could potentially be incorporated into existing diabetes and cardiovascular risk-assessment programs because glucose and triglycerides are already routinely measured in many health-care settings. Nevertheless, its practical value for dementia screening has not yet been established through prospective implementation or cost-effectiveness studies.

However, the TyG index is not a substitute for established clinical assessment or disease-specific Alzheimer's biomarkers. It reflects metabolic health rather than Alzheimer's pathology directly, and its association with cognitive outcomes may be influenced by age, diabetes, obesity, hypertension, dyslipidemia, cardiovascular disease, medications, lifestyle, socioeconomic factors, and other sources of confounding. Differences in study populations, TyG thresholds, laboratory methods, and cognitive outcomes also limit the generalizability of a single cut-off value. Further validation in LMIC populations is therefore required before TyG can be incorporated into routine dementia screening. Any future implementation should use population-specific thresholds, standardized laboratory procedures, clear referral pathways, and appropriate ethical safeguards.

Overall, the TyG index is a promising adjunctive marker of metabolic risk that warrants further investigation in dementia prevention and early-risk assessment. Its potential role in LMICs lies in its low cost and compatibility with existing metabolic health programs, rather than in its ability to diagnose Alzheimer's disease independently. Prospective validation, implementation research, health-economic evaluation, and locally appropriate cut-off values will be necessary before large-scale screening can be recommended.

Literature selection and evidence appraisal

This editorial used a focused narrative literature-selection approach. PubMed/MEDLINE and Google Scholar were searched using combinations of the terms "triglyceride-glucose index," "TyG," "insulin resistance," "cognitive decline," "dementia," "Alzheimer's disease," "blood-based biomarkers," "primary care," and "low- and middle-income countries." Priority was given to original prospective cohort studies, population-based studies, systematic reviews and meta-analyses, authoritative clinical guidance, and peer-reviewed literature relevant to Pakistan and other LMIC settings. Foundational mechanistic studies were retained where necessary to explain biological plausibility. Evidence was interpreted according to study design, effect estimates, adjustment for confounders, and stated limitations. This is a narrative editorial rather than a systematic review; therefore, no new pooled estimate was generated. This approach distinguishes evidence of association from evidence sufficient to support clinical diagnostic use.

Practical implementation in LMIC settings

Population-specific cut-offs. No universal TyG threshold for Alzheimer's disease screening can currently be recommended. Candidate thresholds should be derived and externally validated in the target population and evaluated against standardized cognitive outcomes and, where feasible, disease-specific Alzheimer's biomarkers. Diagnostic performance should be assessed using sensitivity, specificity, predictive values, and calibration across age, sex, diabetes status, and urban/rural populations.

Proposed screening pathway. A feasible pathway would incorporate fasting glucose and triglyceride measurements into existing diabetes, hypertension, cardiovascular-risk, or older-adult health visits. TyG should be interpreted alongside age, vascular risk factors, functional status, and a validated brief cognitive assessment. Individuals with concerning cognitive symptoms or abnormal cognitive screening should undergo clinical assessment and referral according to local capacity. Disease-specific blood biomarkers, CSF analysis, and neuroimaging should remain specialist or confirmatory investigations according to clinical indication and availability. Current Alzheimer's Association guidance emphasizes that disease-specific blood biomarkers should be used within a comprehensive clinical evaluation and appropriate specialist-care context [13].

Feasibility across LMIC settings. In settings with established laboratory networks, TyG can be calculated from routine metabolic testing with minimal additional infrastructure. In rural or lower-resource areas, implementation may require reliable specimen transport, laboratory quality assurance, standardized fasting instructions, staff training, and simple calculation tools. Integration with established noncommunicable-disease programs is likely to be more feasible than establishing a separate dementia-screening service.

Health-economic considerations. The economic rationale for TyG is based on the low incremental cost of using routinely measured glucose and triglycerides; it should not be described as proven cost-effective for dementia screening. Formal economic evaluations should compare usual care with TyG-assisted risk stratification and alternative cognitive or biomarker pathways, including laboratory costs, referral and confirmatory-testing costs, false-positive and false-negative consequences, and downstream effects on patients and caregivers.

Ethical considerations. Large-scale screening requires informed communication, privacy protection, equitable access to follow-up, and careful management of stigma. Because TyG is not specific for Alzheimer's disease, an elevated result should not be communicated as evidence that an individual has AD. Programs should explain uncertainty and the possibility of false-positive and false-negative results. Combining metabolic and cognitive information also requires appropriate data-governance safeguards.

Confounding and causal limitations

The evidence linking TyG with cognitive outcomes is predominantly observational. Associations may be partly explained by shared risk factors, including age, obesity, diabetes, hypertension, dyslipidemia, cardiovascular disease, smoking, physical inactivity, socioeconomic conditions, education, APOE genotype, and medication use. Residual confounding, reverse causation, and survival bias cannot be excluded. Considerable heterogeneity also exists in TyG categorization, laboratory measurement, cognitive assessment, and statistical adjustment. Consequently, current evidence supports risk association rather than causality, and there is insufficient evidence to claim that modifying TyG itself prevents Alzheimer's disease.

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