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TAKE-HOME MESSAGE: Blood-based biomarkers significantly distinguished cognitive status in a population with low educational attainment.

BACKGROUND

Blood-based biomarkers (BBM) are reliable indicators of cognitive decline in Alzheimer's disease. Tests like the Mini-Mental State Examination (MMSE) and the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) are tools for assessing cognitive impairment. Objective: To correlate BBM (pTau217, GFAP, NfL, Aβ42, Aβ40) with MMSE and CERAD Word List Delayed Recall (CERAD-WL), in a low educational attainment cohort from low-and middle-income country.

METHODS

This cross-sectional study included 96 participants from the Cog-Aging cohort (2014-2024) who underwent medical and neuropsychological assessments as well as blood sampling analysis using single-molecule array (Simoa®). MMSE and CERAD-WL were analyzed as continuous and dichotomous variables, using cut-offs: 3 for CERAD-WL and 24/20 (literate/illiterate) for MMSE. BBM and cognitive performance were analysed using Mann-Whitney, partial correlations (adjusted for age, education and Glomerular Filtration Rate (eGFR)) and linear regression to investigate predictors (MMSE (score), Sex, Age, Education, eGFR) of log-transformed pTau217.

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RESULTS

The mean age was 75.09 (SD 6.3), median years of education 4 (IQR 7.25), and 54.2% were female. Sample included dementia of the Alzheimer's type (n=19), mild cognitive impairment (n=54) and cognitively unimpaired (n=23) (Table 1). Levels of pTau217 (p=0.003), pTau217/Aβ42 (p=0.009), GFAP (p=0.003) and NfL (p=0.013) were higher in participants below CERAD-WL cut-off. Similarly, pTau217 (p=0.002), pTau217/Aβ42 (p=0.002) and GFAP (p<0.001) differed by MMSE status (Figure 1). Adjusted for confounders, MMSE showed a strong correlation with pTau217 (rho=-0.522), pTau217/Ab42 (rho=-0.511) and GFAP (rho=-0.509), but weak with NfL (rho=-0.267) and Ab42/Ab40 (rho=0.214). CERAD-WL showed a moderate correlation with pTau217 (rho=-0.459), pTau217/Ab42 (rho=-0.375) and GFAP (rho=-0.453) (Figure 2). Linear regression identified MMSE as the strongest predictor (β=-0.558) of pTau217 levels, followed by education (β=0.364).

Table 1. Demographic and clinical characteristics.

	DAT (N=19)	MCI (N=54)	CU (N=23)	Overall (N=96)
Female, n (%)	9 (47.4%)	28 (51.9%)	15 (65.2%)	52 (54.2%)
Race				
White, n (%)	6 (31.6%)	19 (35.2%)	9 (39.1%)	34 (35.42%)
Non-white, n (%)	6 (31.6%)	31 (57.4%)	11 (47,8%)	48 (50.0%)
Missing	7 (36.8%)	4 (7.4%)	3 (13.0%)	14 (14.58%)
Positive Family History, n (%)	10 (52.6%)	22 (41.5%)	9 (39.1%)	41 (43.2%)
Age (years)	76.9 (7.8)	75.7 (5.9)	72.3 (4.9)	75.1 (6.3)
1+ APOE ε4 alleles, n (%)	12 (33.3%)	22 (22.0%)	4 (8.7%)	38 (20.9%)
Education (years)	7.0 (6.2)	5.9 (4.5)	9.7 (6.4)	7.0 (5.5)
MMSE (score)	17.6 (5.2) [6.0, 25.0]	24.1 (3.0) [17.0, 30.0]	27.0 (2.3) [22.0, 30.0]	23.5 (4.6) [6.0, 30.0]
Impaired MMSE, n (%)	18 (94.7%)	28 (51.9%)	3 (13.0%)	49 (51.1%)
CERAD (score)	0.8 (1.3) [0.0, 5.0]	3.1 (2.5) [0.0, 9.0]	6.4 (1.9) [3.0, 10.0]	3.4 (2.9) [0.0, 10.0]
Impaired CERAD, n (%)	18 (94.7%)	32 (59.3%)	2 (8.7%)	52 (54.2%)
pTau217 (pg/mL)	1.21 (0.58)	0.53 (0.38)	0.34 (0.20)	0.62 (0.50)
pTau217 / Aβ42	0.22 (0.14)	0.10 (0.10)	0.052 (0.032)	0.112 (0.112)
NfL (pg/mL)	28.73 (15.0)	20.36 (8.58)	17.56 (6.79)	21.34 (10.46)
GFAP (pg/mL)	262.4 (94.55)	159.8 (70.72)	132.7 (54.78)	173.6 (85.27)
Aβ42 / Aβ40	0.049 (0.011)	0.052 (0.014)	0.057 (0.013)	0.053 (0.013)

Note: Continuous variables are expressed as mean (standard deviation) and categorical variables as frequency (percentage).
Abbreviations: DAT, dementia of the Alzheimer's type; MCI, mild cognitive impairment; CU, cognitively unimpaired; APOE, apolipoprotein E; MMSE, Mini-Mental State Examination; CERAD, Consortium to Establish a Registry for Alzheimer's Disease. pTau217, tau phosphorylated at threonine 217; Aβ, amyloid-β; GFAP, glial fibrillary acidic protein; NfL, neurofilament light chain.

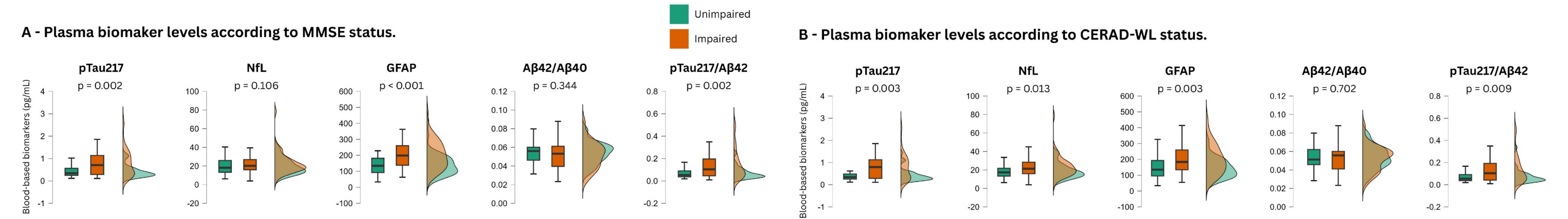


Figure 1. Plasma biomarker levels according to MMSE (A) and CERAD-WL (B) status. Cut-offs: 3 for CERAD-WL and 24/20 (literate/illiterate) for MMSE.

CONCLUSIONS

BBM significantly distinguished cognitive impairment. pTau217 showed the strongest correlations with MMSE and CERAD-WL. Linear regression model suggests cognitive performance and education influence the estimation of neuropathology in this population.

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