

BACKGROUND

- Blood-based biomarkers (BBMs) are increasingly critical for Alzheimer's Disease (AD) diagnosis.
- The interference of systemic factors on plasma BBM levels remains underinvestigated, particularly in Low- and Middle-Income Countries (LMICs).

METHODS

- **Study Design:** Cross-sectional analysis (n=332).
- **Measurements:** Plasma p-tau217, GFAP, Aβ42, and Aβ40 quantified via Simoa®; APOE genotyping via real-time PCR.
- **Stratification:** Kidney impairment (eGFR < 60 mL/min/1.73m²); Obesity (BMI ≥ 30 kg/m²).
- **Analysis:** Adjusted Multivariable Linear Regressions (MLR) and Generalized Linear Models (GLM).

CONCLUSIONS

- Renal function directly affects individual p-tau217, p-tau217/Aβ42, and GFAP levels.
- BMI independently influences GFAP levels.
- **Clinical Implication:** Systemic factors confound BBM interpretation. The Aβ42/Aβ40 ratio should be prioritized in clinical settings due to its resilience.

The plasma Aβ42/Aβ40 ratio is the biomarker most resilient to changes in BMI and eGFR, while p-tau217, GFAP, and p-tau217/Aβ42 are significantly altered by them.

RESULTS

Participants had mean age of 76.3 (SD 7.0); sample included 95 with kidney impairment and 76 with obesity (**table 1**). p-tau217, GFAP, and p-tau217/Aβ42 were significantly higher in kidney impairment (p < 0.035) (**figure 2**). Obese individuals presented lower p-tau217 (p = 0.016) and GFAP (p < 0.001). eGFR correlated with p-tau217 (rho = -0.254) and GFAP (rho = -0.281); BMI correlated with p-tau217 (rho = -0.157) and GFAP (rho = -0.289) (all p < 0.01) (**figure 1**). The Aβ42/Aβ40 ratio remained stable across kidney (p = 0.717) and obesity (p = 0.490) status. MLR identified eGFR as an independent predictor of Log-p-tau217 (β = -0.255), Log-GFAP (β = -0.200), and p-tau217/Aβ42 (β = -0.255) (all p < 0.001). BMI independently predicted only Log-GFAP (β = -0.222, p < 0.001). In GLM analysis, the Aβ42/Aβ40 was independent of eGFR (p = 0.659) and BMI (p = 0.413), with APOEε4 being its only significant predictor (p < 0.001).

Table 1: Demographic and Clinical Characteristics

Variable	CKD 0 (eGFR ≥ 60)	CKD 1 (eGFR < 60)	p (CKD)	Non-Obese (BMI < 30)	Obese (BMI ≥ 30)	p (Obesity)
N	212	95	-	256	76	-
Age (years), mean (SD)	74.93 (6.32)	79.29 (7.41)	< 0.001 ^a	76.65 (7.10)	74.63 (6.39)	0.030 ^b
Female Sex, n (%)	139 (65.6%)	64 (67.4%)	0.758 ^c	169 (66.0%)	59 (77.6%)	0.055 ^c
Education (years), mean (SD)	5.65 (4.49)	5.61 (5.26)	0.374 ^d	6.20 (5.08)	4.55 (3.69)	0.047 ^d
Body Mass Index (kg/m²), mean (SD)	27.53 (4.59)	26.29 (3.91)	0.026 ^b	25.19 (3.11)	32.99 (2.62)	< 0.001 ^d
ApoE ε4 Positive, n (%)	61 (31.1%)	32 (35.2%)	0.496 ^c	76 (33.8%)	17 (25.8%)	0.219 ^c
Clinical Diagnosis, n (%)			0.076 ^c			0.095 ^c
Cognitively Unimpaired	64 (30.2%)	22 (23.2%)		70 (27.3%)	27 (35.5%)	
Mild Cognitive Impairment	95 (44.8%)	39 (41.1%)		108 (42.2%)	35 (46.1%)	
Alzheimer's Disease (AD)	47 (22.2%)	28 (29.5%)		68 (26.6%)	10 (13.2%)	

(a) Welch's T-test was applied when Levene's test indicated unequal variances.

(c) Pearson's Chi-square test (χ²) for categorical variables.

(b) Student's T-test for independent samples.

(d) Mann-Whitney U test for non-normally distributed continuous variables.

Figure 2: Raincloud Plots

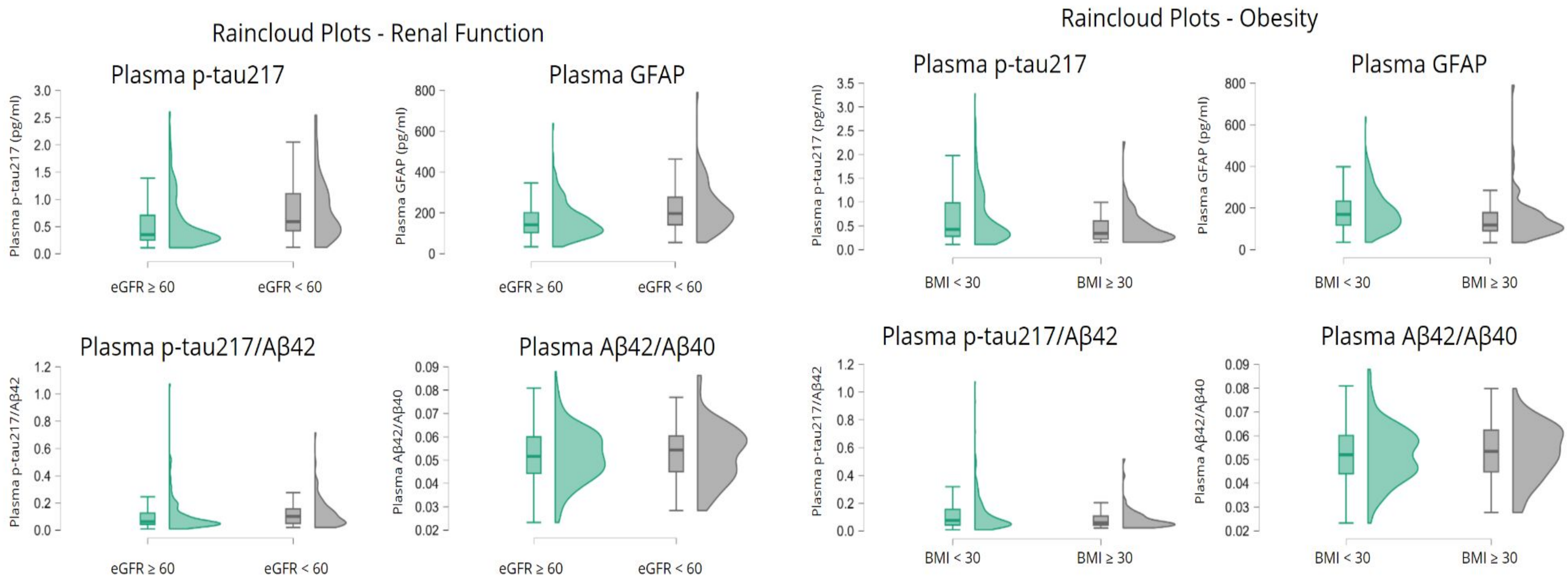
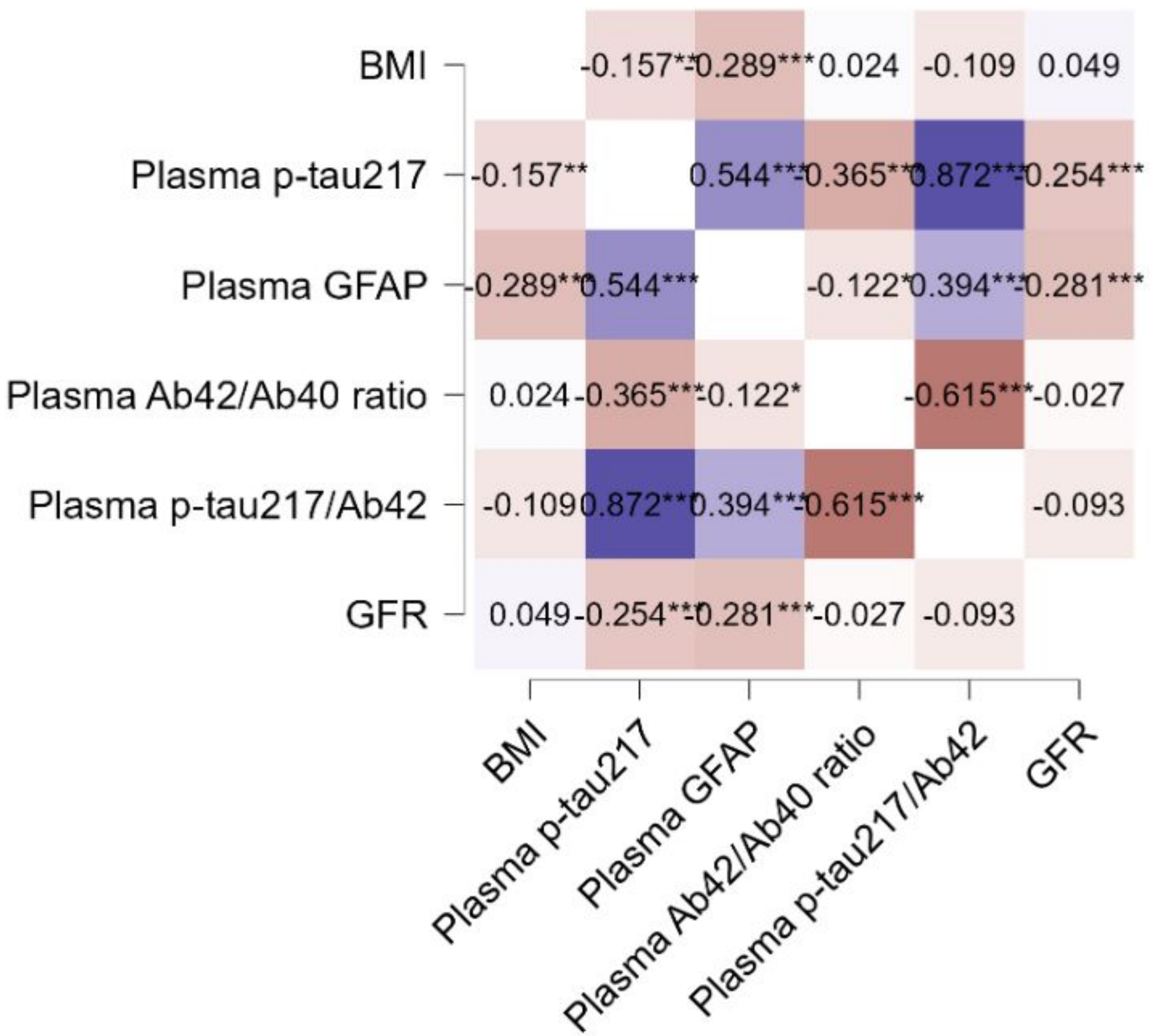


Figure 1 - Spearman's rho Heatmap



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