

Background

Red blood cell (RBC) indices, including erythrocytes, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red cell distribution width (RDW), are routine blood measures that reflect overall physiology, have been linked to longevity and are considered putative markers of biological aging. Although established aging biomarkers such as PhenoAge have been linked to cognitive decline and Alzheimer’s disease risk, it remains unclear whether standard RBC indices are related to cognitive health.

Method

Clinical evaluations and complete blood count (CBC) measures were obtained on 30 adults without cognitive impairment and 27 adults with cognitive impairment (i.e. diagnosis of mild cognitive impairment or dementia). A subset (N=32) completed the Montreal Cognitive Assessment (MoCA). RBC indices were log transformed prior to analyses. Differences in RBC indices between the cognitively unimpaired and impaired groups were assessed using linear regression models adjusted for age, sex, and education. Associations between RBC indices and MoCA total scores were evaluated with linear regression models adjusted for age, sex, and education.

Demographic

Variables	Cognitively Unimpaired (CU)	Cognitively Impaired (CI)
Full Cohort, N (%)	30 (52.6%)	27 (47.4%)
Age (years), mean ± SD	69.93 ± 10.06	71.74 ± 7.85
Education, n(%)		
• < 4 years of college	9 (30%)	8 (29.6%)
• 4-year college	10 (33.3%)	7 (25.9%)
• Graduate or professionals	11 (36.7%)	12 (44.4%)
Sex Assigned at Birth, n (%)		
• Male	10 (33.3%)	12 (44.4%)
• Female	20 (66.7%)	15 (55.6%)
Race, n (%)		
• Asian	9 (30.0%)	2 (7.4%)
• Black or African-American	2 (6.7%)	1 (3.7%)
• Hispanic or Latino	1 (3.3%)	-
• Middle Eastern or North African	1 (3.3%)	1 (3.7%)
• White	17 (56.7%)	22 (81.5%)
• Other	-	1 (3.7%)
RBC Indices, median (IQR)		
• Erythrocytes	4.40 (0.57)	4.6 (0.82)
• Hemoglobin	13.2 (1.9)	13.5 (2.0)
• Hematocrits	40.0 (4.8)	42.7 (7.2)
• MCV	92.8 (6.6)	92.8 (7.1)
• MCH	30.2 (2.1)	29.8 (3.1)
• MCHC	32.6 (1.3)	32.1 (1.4)
• RDW	13.15 (1.2)	13.6 (1.2)
Subset Cohort, n (%)	17 (56.7%)	15 (55.6%)
MoCA Total Score, mean ± SD	26.18 ± 1.78	29.3 (25.4)

RBC Indices and Cognitive Diagnosis

RBC Indices	β (95% CI), p-value
Erythrocytes	β = 0.069 (95% CI 0.012 to - 0.126), p = 0.018*
Hemoglobin	β = 0.017 (95% CI -0.038 to 0.073), p = 0.530
Hematocrits	β = 0.037 (95% CI -0.018 to 0.092), p = 0.178
MCV	β = -0.031 (95% CI -0.065 to 0.002), p = 0.066
MCH	β = -0.052 (95% CI -0.086 to - 0.017), p = 0.004*
MCHC	β = -0.020 (95% CI -0.037 to -0.003), p = 0.023*
RDW	β = 0.039 (95% CI -0.003 to 0.081), p = 0.065

RBC Indices and MOCA Total Score

*Note: β (95% CI) and p-values derived from linear regression models examining the associations between cognitive group or MoCA total score with RBC indices adjusting for age, sex, and education. *p<0.05

RBC Indices	β(95% CI), p-value
Erythrocytes	β = -0.002 (95% CI -0.004 to 0.002), p = 0.396
Hemoglobin	β = -0.001 (95% CI -0.003 to 0.002), p = 0.580
Hematocrits	β = -0.001 (95% CI -0.003 to 0.002), p = 0.531
MCV	β = 0.000 (95% CI -0.001 to 0.002), p = 0.573
MCH	β = 0.001 (95% CI -0.001 to - 0.002), p = 0.511
MCHC	β = 0.000 (95% CI -0.037 to -0.003), p = 0.754
RDW	β = -0.001 (95% CI -0.002 to 0.001), p = 0.380

Result

Compared to cognitively unimpaired participants, cognitively impaired individuals showed higher erythrocyte levels (β=0.069, p=0.018) and lower MCH (β=-0.052, p=0.004) and MCHC (β=-0.020, p=0.023). No RBC indices were significantly associated with MoCA performance (all p>0.05)

Conclusion

Select RBC indices differed by cognitive impairment status, suggesting potential utility as accessible markers of cognitive aging. However, the lack of association with cognitive test performance indicates that these measures may reflect diagnostic status rather than severity. Larger longitudinal studies are needed to confirm these findings and evaluate prognostic value.

Limitation

Modest sample size (N= 57)

Citation

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