



## Letter to the Editor

Plasma  $\beta$ -amyloid1–42 reference values

## ARTICLE INFO

## Keywords:

$\beta$ -Amyloid  
Reference values  
Dementia.

## Dear Editor,

Zecca et al. evaluated plasma  $\beta$ -Amyloid1–42 (A $\beta$ 1–42) concentrations in 245 cognitively normal subjects to determine reference values of Alzheimer's disease. [1]. The mean concentration of plasma A $\beta$ 1–42 increased by aging, although there was no significant difference in the mean concentration of plasma A $\beta$ 1–42 between the adult (35 to 64 years old) and the old (65 to 89 years old) groups. The authors presented 8.12 (95% CI 6.77–9.45) to 29.00 (95% CI 27.01–31.00) pg/mL as a reference value from the lower to upper limit. I have two concerns about this study.

First, Lövheim et al. examined plasma concentration of amyloid  $\beta$ 40 (A $\beta$ 40) and amyloid  $\beta$ 42 (A $\beta$ 42) as biomarkers for screening Alzheimer's disease (AD) development [2]. A total of 339 preclinical AD cases, with an average of 9.4 years before AD diagnosis, and 339 age- and sex-matched dementia-free controls were set for the analysis. There were no significant differences in the mean values of plasma concentrations of free A $\beta$ 40 and A $\beta$ 42 between preclinical AD cases and dementia-free controls, although stratification by sex and age were conducted. In addition, plasma concentrations of free A $\beta$ 40 and A $\beta$ 42 did not change in the years preceding AD diagnosis by longitudinal analysis. Taken together, they concluded that free plasma A $\beta$  was not a useful biomarker for screening AD development.

In contrast, Nakamura et al. demonstrated the measurement of high-performance plasma amyloid- $\beta$  biomarkers to know the ability of amyloid- $\beta$  precursor protein (APP) 669–711/amyloid- $\beta$  (A $\beta$ )1–42 and A $\beta$ 1–40/A $\beta$ 1–42 ratios, and their composites to predict individual brain amyloid- $\beta$ -positive or -negative status [3]. Cognitively normal individuals, individuals with mild cognitive impairment and individuals with Alzheimer's disease were included for the analysis, and the composite biomarker showed highest areas under the receiver operating characteristic curves with an accuracy of approximately equal to 90%

when using PIB-PET as a gold standard. They used individual brain amyloid- $\beta$  binary status as the target indicator, and strict statistical procedures were adopted for the analysis. Plasma biomarkers were closely correlated with amyloid- $\beta$ -PET burden and levels of A $\beta$ 1–42 in cerebrospinal fluid, and the information would support data by Zecca et al. as the useful information for screening Alzheimer's disease. Anyway, validation study on cutoff value should be conducted by further studies.

## Disclosure statement

The author has indicated no financial support.

## Conflicts of interest

There is no conflict of interest in this study.

## References

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