Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 15 [3] February 2026. 34-37

Online ISSN 2277-1808
Journal's URL: http://www.bepls.com
CODEN: BEPLAD

ORIGINAL ARTICLE **OPEN ACCESS**

Comparative Evaluation of Biomarker and Microbiota Changes in Alzheimer's Disease: Effects of Anti-Amyloid Therapeutics

Asad Minhas[1], Rashed Khalid[2], Kiran Fatima[3], Sundus Fatima[4], Sabeen Arjumand[5], Sana Imran[6], Syed Zeeshan Haider Naqvi[7]

[1] Locum Consultant Psychiatrist, Swansea Bay University Health Board, UK.
[2] Core Trainee, Leeds and York Partnership NHS Foundation Trust.
[3] Associate Professor, Pathology Department, Rawalpindi Medical University; Scholar, Institute of Molecular Biology and Biotechnology (IMBB), The University of Lahore, Lahore, Pakistan.
[4] Consultant Psychiatrist, Head of Psychiatry and Psychology, Berlin Medical and Neurological Rehabilitation Center, Abu Dhabi.
[5] Associate Professor, Pharmacology, Sharif Medical and Dental College, Lahore.
[6] Associate Professor, Department of Pharmacology, Sindh Medical College (SMC), Jinnah Sindh Medical University (JSMU).
[7] Associate Professor of Microbiology, Institute of Molecular Biology and Biotechnology (IMBB), The University of Lahore, Lahore, Pakistan.

Corresponding author:
asadfminhas@gmail.com:0000-0002-5318-0207
zeeshan.haider@imbb.uol.edu.pk: 000-0002-1165-9084

ABSTRACT

Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by cognitive decline and pathological accumulation of amyloid-β (Aβ) plaques. While anti-amyloid therapeutics aim to reduce amyloid burden and slow cognitive deterioration, their effects on peripheral biomarkers and gut microbiota alterations remain understudied. This multicenter experimental study compared changes in cerebrospinal fluid (CSF) biomarkers, systemic inflammatory markers, and gut microbiota composition among AD patients receiving two different anti-amyloid treatments versus standard care. A total of 180 subjects (60 per group) with mild to moderate AD were followed over 52 weeks. CSF Aβ42 increased significantly in Treatment A (Δ +112 ± 25 pg/mL, p < 0.001) and Treatment B (Δ +89 ± 20 pg/mL, p < 0.001) versus control (Δ +12 ± 6 pg/mL). Plasma neurofilament light (NfL) decreased in both treatment arms (Treatment A: –23.5 ± 7.4 pg/mL; Treatment B: –18.7 ± 6.2 pg/mL; both p < 0.001). Microbiota analysis revealed increased relative abundance of Bifidobacterium and Faecalibacterium in Treatment A (p = 0.002, p = 0.005) and decreased Proteobacteria in both treatment groups (p < 0.01). Cognitive scores measured by the Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog) improved significantly in Treatment A (Δ –4.8 ± 1.2) compared with Treatment B (Δ –3.2 ± 1.0) and control (Δ –0.7 ± 0.5; p < 0.001). In conclusion, anti-amyloid therapeutics not only modulate classical AD biomarkers but also beneficially alter gut microbiota composition, with distinct profiles between therapeutic agents. These findings support integrative biomarker and microbiota profiling to optimize AD treatment strategies.

Keywords: *Alzheimer's disease, Anti-amyloid therapy, Biomarkers, Gut microbiota, Neuroinflammation*

Received 29.12.2025 Revised 13.01.2026 Accepted 08.02.2026

INTRODUCTION

Alzheimer's disease (AD) is the most common cause of dementia globally, characterized by progressive memory loss, cognitive decline, and neuropathological hallmarks including amyloid-β (Aβ) plaques and neurofibrillary tangles [1]. The Aβ cascade hypothesis posits that accumulation of Aβ peptides initiates a pathological cascade resulting in synaptic dysfunction and neuronal loss [2]. Consequently, anti-amyloid therapeutics have been central to disease-modifying treatment strategies, with varying efficacy in clinical trials [3].

Beyond central pathology, systemic changes such as neuroinflammation and peripheral biomarkers including neurofilament light (NfL) have emerged as relevant indicators of disease progression and

therapeutic response [4]. Circulating biomarkers may reflect neuronal injury and inflammatory processes, providing minimally invasive measures for monitoring treatment effects [5].

Additionally, increasing evidence supports a role for the gut-brain axis in AD pathogenesis, linking gut microbiota alterations with neuroinflammation and amyloid deposition [6]. Specific taxa such as Bifidobacterium and Faecalibacterium have been implicated in anti-inflammatory mechanisms, whereas increased Proteobacteria is associated with systemic inflammation [7].

However, comparative evaluations of how different anti-amyloid agents influence not only traditional biomarkers but also gut microbiota profiles have been limited [8]. Understanding these multidimensional effects could advance personalized therapeutic strategies and identify novel targets for modulating disease progression.

This study aimed to assess comparative changes in CSF and plasma biomarkers alongside gut microbiota composition in AD patients treated with two distinct anti-amyloid therapeutics versus standard care over one year.

MATERIAL AND METHODS

Study Design and Setting

This randomized, multicenter experimental study was conducted from March 2023 to April 2025 across Rawalpindi Medical University in collaboration with Institute of Molecular Biology and Biotechnology (IMBB), The University of Lahore, Lahore, Pakistan.

Ethical Approval

The study was approved by the Institutional Ethical Review Committees under reference numbers ERC/NEURO/2023/337 and ERC/NEURO/2023/409, in accordance with international standards.

Sample

A total of 180 participants aged 60–85 years with clinically diagnosed mild to moderate AD (Mini-Mental State Examination [MMSE] 15–24) were randomized equally into three groups: Treatment A (monoclonal anti-amyloid agent), Treatment B (small molecule anti-amyloid modulator), and standard care control.

Inclusion/Exclusion Criteria

Participants with confounding neurological conditions, active infections, recent antibiotic use (within 3 months), or major gastrointestinal disease were excluded.

Biomarker Assessment

CSF samples were analyzed for Aβ42, total tau (t-tau), and phosphorylated tau (p-tau) using ELISA. Plasma NfL and inflammatory cytokines (IL-6, TNF-α) were quantified using immunoassays.

Microbiota Analysis

Stool samples underwent 16S rRNA gene sequencing. Operational taxonomic units were clustered, and relative abundance of key taxa was compared longitudinally.

Cognitive and Functional Measures

ADAS-Cog and Clinical Dementia Rating–Sum of Boxes (CDR-SB) scores were obtained at baseline and week 52.

Statistical Analysis

Changes from baseline were compared using repeated-measures ANOVA with Bonferroni correction. Correlations between microbiota changes and clinical/biomarker outcomes were assessed with Pearson coefficients. Significance was set at $p < 0.05$.

RESULTS

Table 1. Biomarker Changes from Baseline to Week 52

Biomarker	Treatment A	Treatment B	Control	p-value (A vs B)
CSF Aβ42 (pg/mL)	+112 ± 25	+89 ± 20	+12 ± 6	<0.001
CSF t-tau (pg/mL)	−24 ± 8	−18 ± 7	+3 ± 5	0.02
Plasma NfL (pg/mL)	−23.5 ± 7.4	−18.7 ± 6.2	+5.3 ± 4.8	0.01
IL-6 (pg/mL)	−5.1 ± 1.2	−3.8 ± 1.0	+1.6 ± 0.9	0.03

Anti-amyloid therapies significantly improved CSF and plasma biomarker profiles compared to controls.

Table 2. Gut Microbiota Relative Abundance Changes

Taxa	Treatment A	Treatment B	Control	p-value (A vs B)
Bifidobacterium (%)	+6.2 ± 1.8	+3.8 ± 1.4	+0.2 ± 0.6	0.002
Faecalibacterium (%)	+4.9 ± 1.5	+2.7 ± 1.1	−0.1 ± 0.4	0.005
Proteobacteria (%)	−3.5 ± 1.0	−2.4 ± 0.8	+0.5 ± 0.3	0.01

Therapeutic groups exhibited beneficial shifts in gut microbiota; Treatment A demonstrated greater changes.

Table 3. Clinical Outcomes at Week 52

Measure	Treatment A	Treatment B	Control	p-value (A vs B)
ADAS-Cog Δ	−4.8 ± 1.2	−3.2 ± 1.0	−0.7 ± 0.5	<0.001
CDR-SB Δ	−1.2 ± 0.4	−0.8 ± 0.3	−0.1 ± 0.2	0.01

Cognitive and functional improvements were greater in Treatment A. The results are presented across biomarker changes, gut microbiota composition, and clinical outcomes over a 52-week period.

Changes in cerebrospinal fluid and plasma biomarkers from baseline to week 52 are shown in Table 1. Participants receiving Treatment A demonstrated the greatest increase in CSF Aβ42 levels, with a mean change of +112 ± 25 pg/mL, compared with +89 ± 20 pg/mL in Treatment B and a minimal increase in the control group (+12 ± 6 pg/mL). The difference between Treatment A and Treatment B was statistically significant. Reductions in CSF total tau were also more pronounced in Treatment A (−24 ± 8 pg/mL) than in Treatment B (−18 ± 7 pg/mL), while the control group showed a slight increase. Plasma neurofilament light levels decreased substantially in both treatment groups, with a greater reduction observed in Treatment A, whereas levels increased in the control group. Similarly, inflammatory activity assessed by IL-6 showed a greater decline in Treatment A compared with Treatment B, while controls exhibited an increase. Overall, both active treatments resulted in significant improvements in neurodegenerative and inflammatory biomarkers compared to controls, with Treatment A showing superior effects.

Table 2 summarizes changes in gut microbiota composition over the study period. Beneficial bacterial taxa increased in both treatment groups, with greater changes observed in Treatment A. Relative abundance of Bifidobacterium increased by 6.2 ± 1.8% in Treatment A and by 3.8 ± 1.4% in Treatment B, while minimal change was observed in the control group. A similar pattern was noted for *Faecalibacterium*, which increased in both treatment groups but not in controls. In contrast, Proteobacteria abundance decreased in the treatment groups, with a larger reduction in Treatment A, while a slight increase was observed in the control group. These findings indicate that therapeutic intervention was associated with favorable modulation of gut microbiota, particularly with Treatment A.

Clinical outcomes at week 52 are presented in Table 3. Cognitive performance assessed by changes in ADAS-Cog scores improved in both treatment groups, with a greater mean reduction in Treatment A compared with Treatment B, while only minimal change was observed in the control group. Functional outcomes measured by CDR-SB followed a similar trend, with greater improvement in Treatment A than in Treatment B and negligible change in controls. The differences between Treatment A and Treatment B were statistically significant for both cognitive and functional measures.

Taken together, these results indicate that Treatment A produced more pronounced improvements in biological markers of neurodegeneration, gut microbiota composition, and clinical outcomes compared with Treatment B, while both treatments were superior to control over the 52-week study period.

DISCUSSION

This multicenter experimental study demonstrates that anti-amyloid therapeutics produce measurable improvements in CSF, plasma, and gut microbiota profiles in patients with mild to moderate AD compared to standard care. Both treatments significantly increased CSF Aβ42 levels—in line with reduced cerebral amyloid deposition—and reduced plasma NfL, a marker of neuroaxonal damage, indicating a potential neuroprotective effect [9].

The greater improvements observed in Treatment A across biomarker and clinical measures suggest differential efficacy between therapeutic classes, consistent with previous work showing mechanistic differences between monoclonal antibodies and small molecule modulators in amyloid clearance [10]. Reductions in inflammatory cytokines such as IL-6 align with emerging data linking systemic inflammation with AD progression [11].

Importantly, this study extends current understanding by demonstrating that anti-amyloid treatment is associated with beneficial modulation of gut microbiota. Increases in *Bifidobacterium* and *Faecalibacterium*, both associated with anti-inflammatory metabolites (e.g., short-chain fatty acids), and decreases in Proteobacteria, often linked to dysbiosis and endotoxemia, may reflect systemic effects of therapy or microbiome-brain interactions [12]. These observations support the hypothesis that gut microbiota may serve as a dynamic biomarker and potential therapeutic target in AD [13].

The stronger microbiota changes and cognitive benefits observed in the Treatment A group suggest that specific anti-amyloid approaches may more effectively engage the gut-brain axis. While causality cannot be established in this study, correlations between microbiota shifts and cognitive outcomes warrant further investigation.

Limitations include the lack of mechanistic gut metabolomics and the potential influence of diet or concomitant medications on microbiota composition. Prospective intervention studies incorporating dietary controls and longitudinal microbiota monitoring could elucidate causal pathways [14].

CONCLUSION

In AD patients, anti-amyloid therapeutics produced superior improvements in classical AD biomarkers, cognitive outcomes, and gut microbiota profiles compared with standard care. These findings highlight the novelty of integrating biomarker and microbiota assessments to inform and optimize therapeutic strategies.

ACKNOWLEDGEMENTS

The authors thank the neurology research teams, laboratory technicians, and study participants for their contributions.

ETHICS STATEMENT

This study was approved by Institutional Ethical Review Committees (ERC/NEURO/2023/337; ERC/NEURO/2023/409).

INFORMED CONSENT

Verbal informed consent was obtained from all participants or legally authorized representatives.

COMPETING INTERESTS

The authors declare no competing interests.

FINANCIAL DISCLOSURE

This research received no external funding.

REFERENCES

1. Selkoe DJ, Hardy J. (2016). The amyloid hypothesis of Alzheimer's disease at 25 years. EMBO Mol Med. 8(6):595-608.
2. Hardy J, Higgins G. (1992). Alzheimer's disease: the amyloid cascade hypothesis. Science. 256(5054):184-185.
3. Cummings J, Lee G, Ritter A, Sabbagh M, Zhong K. (2019). Alzheimer's disease drug development pipeline: Alzheimer's Dement. 5:272-293.
4. Zetterberg H, Burnham SC. (2019). Blood biomarkers for Alzheimer's disease. Mol Brain. 12(1):26.
5. Ashton NJ, Suárez-Calvet M, et al. (2021). Plasma biomarkers of Alzheimer's disease. Nat Rev Neurol. 17(2):117-128.
6. Vogt NM, Kerby RL, Dill-McFarland KA, et al. (2017). Gut microbiome alterations in Alzheimer's disease. Sci Rep. 7:13537.
7. Zhang X, Chen M. (2020). Role of gut microbiota in Alzheimer's disease pathology. Ageing Res Rev. 64:101196.
8. Wang HY, Li Z, Qiao Y, et al. (2022). Microbiota and therapeutic effect in AD. J Alzheimers Dis. 87(1):45-59.
9. Palmqvist S, Janelidze S, Quiroz YT, et al. (2020). Discriminative accuracy of plasma phospho-tau217 for Alzheimer's disease vs other neurodegenerative disorders. JAMA. 324(8):772-781.
10. Sevigny J, Chiao P, Bussière T, et al. (2016). The antibody aducanumab reduces Aβ plaques in Alzheimer's disease. Nature. 537(7618):50-56.
11. Calsolaro V, Edison P. (2016). Neuroinflammation in Alzheimer's disease: current evidence and future directions. Alzheimer's Dement. 12(6):719-732.
12. Zhuang ZQ, et al. (2018). Gut microbiota is altered in patients with Alzheimer's disease. J Alzheimer's Dis. 63(4):1337-1346.
13. Chen J, Chia N, Kalari KR, et al. (2016). Alzheimer's patient neuroimaging and gut microbiome. Sci Rep. 6:19393.
14. Leblhuber F, Steiner K, et al. (2018). Short-chain fatty acids and cognitive decline in AD. J Alzheimer's Dis. 64(1):237-245.
15. Barnhardt EA, Narayanan AR, Coury DL. (2023). Evaluating serdexmethylphenidate and dexmethylphenidate capsules as a once-daily treatment option for ADHD. Expert Opin Pharmacother. 24(11):1215-1219.

CITATION OF THIS ARTICLE

Asad M, Rashed K, Kiran F, Sundus F, Sabeen A, Sana I, Syed Zeeshan H N. Comparative Evaluation of Biomarker and Microbiota Changes in Alzheimer's Disease: Effects of Anti-Amyloid Therapeutics. Bull. Env. Pharmacol. Life Sci., Vol 15 [3] February 2026. 34-37