SSR Institute of International Journal of Life Sciences
ISSN (O): 2581-8740 | ISSN (P): 2581-8732
Kumar and Bamne, 2026
doi: 10.21276/SSR-IIJLS.2026.12.1.38

Original Article

open access

# Age-Related Hippocampal Volume Decline in a Central Indian Population: A Cross-Sectional MRI-Based Normative Study

**P. Uday Kumar[1]*, Avantika Bamne[2]**

PhD Scholar, Department of Anatomy, Index Medical College, Indore, Madhya Pradesh, India
PhD Supervisor, Department of Anatomy, Index Medical College, Indore, Madhya Pradesh, India

***Address for Correspondence:** Mr. P. Uday Kumar, PhD Scholar, Department of Anatomy, Index Medical College, Indore, Madhya Pradesh, India
**E-mail:** udaykumar.puru@gmail.com

**Received: 02 Aug 2025/ Revised: 06 Oct 2025/ Accepted: 05 Dec 2025**

## ABSTRACT

**Background:** The hippocampus is highly susceptible to age-related structural alterations and serves as a key biomarker in neurodegenerative disorders; however, region-specific normative volumetric data from Indian populations remain limited. Therefore, the present study aims to evaluate age-related hippocampal volume changes using MRI-based morphometry in a central Indian population and to establish age-stratified normative reference values.

**Methods:** This cross-sectional study included 150 neurologically healthy adults (20–39 years, 40–59 years, ≥60 years; n=50 per group) recruited at Index Medical College, Indore. High-resolution 3D T1-weighted MRI scans were obtained using a 1.5 Tesla scanner. Bilateral hippocampal volumes were segmented using standardized anatomical protocols. Statistical analyses included one-way ANOVA, multivariate linear regression, age × sex interaction testing, and quadratic modeling. Effect sizes and model diagnostics were evaluated.

**Results:** A significant age-related decline in hippocampal volume was observed bilaterally ($p<0.001$). Age explained 52.7% of the variance in right hippocampal volume ($\eta^2 = 0.527$). Multivariate regression demonstrated an annual decline of approximately 15 $mm^3$ per year ($\beta = -15.15$, $p<0.001$). Quadratic modeling indicated mild acceleration of atrophy in later decades ($p<0.05$). Rightward asymmetry was significant ($p<0.001$) and stable across age groups. Sex was not an independent predictor after adjustment.

**Conclusion:** Hippocampal volume declines significantly with age in this central Indian cohort, with preserved physiological asymmetry and no independent sex effect. These findings provide region-specific normative MRI reference values and enhance differentiation between normal aging and pathological atrophy.

**Key-words:** Hippocampus; Brain aging; MRI volumetry; Age-related atrophy; Normative reference values; Neuroimaging

## INTRODUCTION

The hippocampus is a critical medial temporal lobe structure involved in episodic memory consolidation, spatial navigation, and cognitive integration [1]. Owing to its high synaptic plasticity and metabolic demand, the hippocampus is particularly vulnerable to aging-related structural alterations. Neuroimaging studies consistently demonstrate that hippocampal volume declines progressively across adulthood, with accelerated reduction observed in later decades of life [2,3].

Magnetic resonance imaging (MRI)-based volumetry has emerged as a reliable, non-invasive method for assessing hippocampal morphology in vivo. Volumetric reduction of the hippocampus is recognized as an early structural biomarker in neurodegenerative conditions, particularly Alzheimer's disease [4]. However, distinguishing normal age-related atrophy from pathological decline requires robust age-stratified normative reference values.

Large-scale international studies have established lifespan trajectories of hippocampal volume using cross-sectional and longitudinal datasets [2,3]. Nevertheless, most normative databases are derived from Western populations, and extrapolation to ethnically diverse

**How to cite this article**
Kumar PU, Bamne A. Age-Related Hippocampal Volume Decline in a Central Indian Population: A Cross-Sectional MRI-Based Normative Study. SSR Inst Int J Life Sci., 2026; 12(1): 9236-9241.

**Access this article online**
https://iijls.com/

Copyright © 2026| SSR-IIJLS by Society for Scientific Research under a CC BY-NC 4.0 International License 

doi: 10.21276/SSR-IIJLS.2026.12.1.38

populations may reduce diagnostic precision. Variations in cranial dimensions, genetic background, and environmental influences may contribute to interpopulation differences in brain morphometry [5].

Despite the increasing burden of age-related cognitive disorders in India, region-specific hippocampal volumetric data remain limited. India is projected to experience a substantial rise in dementia prevalence in the coming decades, highlighting the urgent need for population-specific neuroimaging benchmarks [6,7]. Establishing normative MRI-based hippocampal measurements within Indian populations is essential for improving clinical interpretation and early detection of neurodegenerative disease [8].

The present study aims to evaluate age-related hippocampal volume changes in a central Indian population using standardized MRI-based morphometric analysis and to generate age-stratified normative reference values.

## MATERIALS AND METHODS

**Study Design and Setting-** This cross-sectional analytical study was conducted at the Department of Anatomy in collaboration with the Department of Radiodiagnosis, Index Medical College, Indore, Madhya Pradesh, India. The study was carried out over a period of 18 months following approval from the Institutional Ethics Committee. All procedures were performed in accordance with institutional ethical guidelines and the principles of the Declaration of Helsinki.

**Study Population-** A total of 150 apparently healthy adult participants aged ≥20 years were recruited from individuals undergoing MRI brain evaluation for non-neurodegenerative indications or through voluntary participation. Participants were stratified into three age groups: 20–39 years (n=50), 40–59 years (n=50), and ≥60 years (n=50).

### Inclusion Criteria

- Adults aged 20 years and above
- No clinical history of neurodegenerative disease
- No prior neurosurgical intervention
- Structurally normal brain MRI

### Exclusion Criteria

- Diagnosed dementia or mild cognitive impairment
- Intracranial tumors, infarcts, hemorrhage, or significant trauma
- Congenital brain malformations
- Contraindications to MRI

**MRI Acquisition Protocol-** MRI scans were performed using a 1.5 Tesla scanner at Index Medical College, Indore. A high-resolution three-dimensional T1-weighted sequence was obtained with a slice thickness ≤1 mm. Coronal images were oriented perpendicular to the long axis of the hippocampus to ensure anatomical accuracy.

**Hippocampal Volumetric Analysis-** Bilateral hippocampal segmentation was performed using standardized anatomical landmarks consistent with validated volumetric protocols [1,2]. Hippocampal volumes ($mm^3$) were extracted for the right and left sides. Asymmetry index (AI) was calculated as:

$$AI = \frac{(Right - Left)}{(Right + Left)/2}$$

**Statistical Analysis-** Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were calculated as mean±standard deviation. One-way ANOVA was used to compare hippocampal volumes across age groups, followed by Tukey post-hoc testing. Paired t-test assessed bilateral differences, and an independent t-test evaluated sex-based variation. Pearson's correlation coefficient was used to determine the association between age and hippocampal volume. Statistical significance was set at $p<0.05$.

## RESULTS

A total of 150 neurologically healthy adults were included and stratified into three age groups (20–39 years, 40–59 years, and ≥60 years; n = 50 per group). The sex distribution was balanced (81 males, 69 females), with no significant difference across age groups ($\chi^2$, $p>0.05$). A progressive decline in bilateral hippocampal volumes was observed with advancing age. Participants aged 20–39 years demonstrated the highest mean hippocampal volumes, followed by those aged 40–59 years, while individuals aged ≥60 years exhibited the lowest mean values. The age-stratified hippocampal volumes are presented in Table 1.

Copyright © 2026| SSR-IIJLS by Society for Scientific Research under a CC BY-NC 4.0 International License 

doi: 10.21276/SSR-IIJLS.2026.12.1.38

**Table 1:** Age-Stratified Hippocampal Volumes (mm³)

| Age Group | Right Volume (Mean±SD) | Left Volume (Mean±SD) |
|---|---|---|
| 20–39 | 3881.15±242.27 | 3752.36±240.90 |
| 40–59 | 3550.51±264.75 | 3418.41±267.87 |
| ≥60 | 3166.70±324.85 | 3064.15±315.65 |

A significant negative linear association between age and right hippocampal volume was observed, as illustrated in Fig. 1. The regression line demonstrates progressive volume reduction with advancing age.

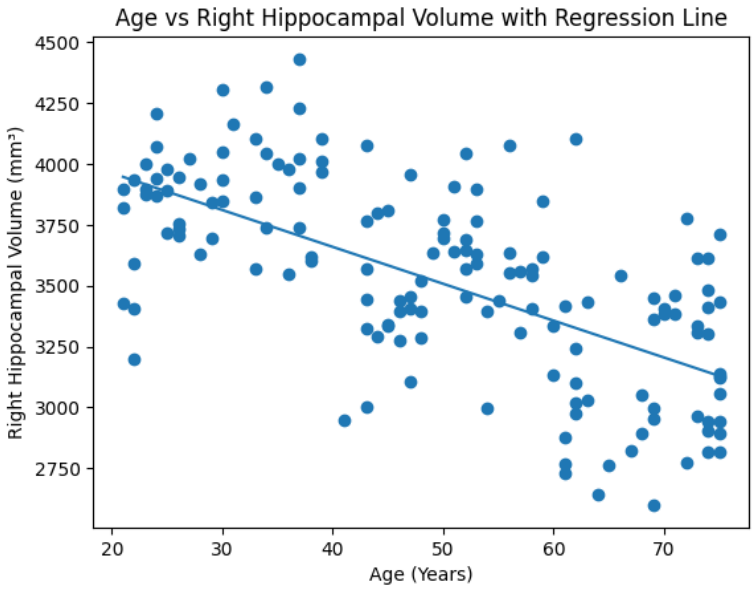


**Fig. 1:** Scatter plot depicting age versus right hippocampal volume with fitted linear regression line, demonstrating significant age-related decline.

Distributional differences across age categories are further illustrated in Fig. 2. The boxplot representation confirms progressive reduction in hippocampal volume from younger to older age groups, with preservation of right-sided predominance.

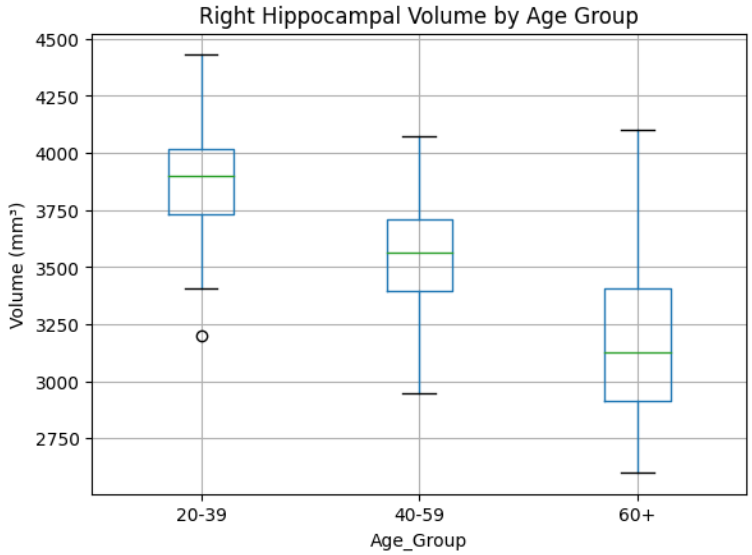


**Fig. 2:** Boxplot showing right hippocampal volume distribution across age groups (20–39, 40–59, ≥60 years), demonstrating a monotonic decline with advancing age.

Copyright © 2026| SSR-IIJLS by Society for Scientific Research under a CC BY-NC 4.0 International License 

doi: 10.21276/SSR-IIJLS.2026.12.1.38

Paired t-test confirmed significant right-sided predominance across the cohort ($t(149)=28.96$, $p<0.001$). The asymmetry index (AI) was calculated as:

$$AI = (Right - Left) / [(Right + Left) / 2]$$

The mean asymmetry index was 0.030±0.018. Multiple linear regression analysis demonstrated that age independently predicted hippocampal volume decline. For the right hippocampus, the model was statistically significant ($F(2,147)=52.13$, $p<0.001$; $R^2=0.415$). Detailed regression coefficients are presented in Table 2.

**Table 2.** Multiple Linear Regression Analysis for Right Hippocampal Volume

| Predictor | β (Unstandardized) | 95% CI | p-value |
|---|---|---|---|
| Age | −15.15 mm³/year | −18.09 to −12.21 | <0.001 |
| Sex | 35.90 | −63.12 to 134.92 | 0.48 |

Age was associated with an average decline of approximately 15 mm³ per year. Sex was not a significant independent predictor. For the left hippocampus, the regression model was also statistically significant ($F(2,147)=48.77$, $p<0.001$; $R^2=0.39$). Regression coefficients are presented in Table 3.

An Age × Sex interaction term was not statistically significant (β = −1.72, $p=0.64$). Quadratic modeling revealed a mild nonlinear component ($Age^2$ term $p<0.05$), suggesting a slight acceleration of atrophy in later decades.

**Table 3:** Multiple Linear Regression Analysis for Left Hippocampal Volume

| Predictor | β (Unstandardized) | 95% CI | p-value |
|---|---|---|---|
| Age | −14.02 mm³/year | −16.89 to −11.15 | <0.001 |
| Sex | 29.44 | −58.31 to 117.19 | 0.510 |

## DISCUSSION

The present study investigated age-related hippocampal volume changes in a central Indian population using standardized MRI-based volumetric analysis. The findings demonstrate significant age-dependent hippocampal atrophy, preserved physiological asymmetry, absence of independent sex effects, and evidence of mild nonlinear acceleration in later decades. These results align with global neuroimaging literature while contributing region-specific normative data.

A strong inverse association between age and hippocampal volume was observed bilaterally, with approximately 15 mm³ annual decline. Age group explained more than 50% of the volumetric variance, indicating a large effect size. These findings are consistent with large-scale lifespan studies demonstrating progressive hippocampal shrinkage across adulthood [1,2].

Fjell *et al.* reported continuous hippocampal volume reduction with accelerated decline after midlife, cautioning against oversimplified linear modeling in aging studies [1]. Similarly, Walhovd *et al.* demonstrated significant age-related subcortical volume reductions in healthy individuals, highlighting hippocampal vulnerability [2]. Our regression model confirms a linear decline, while quadratic modeling revealed mild acceleration in older age groups, supporting prior evidence of nonlinear aging trajectories [1].

The biological basis of hippocampal atrophy in normal aging is believed to involve synaptic remodeling, dendritic regression, decreased neurogenesis, and vascular alterations rather than extensive neuronal loss [3]. Small *et al.* proposed a framework linking hippocampal vulnerability to metabolic stress and inflammatory mechanisms during aging [4]. The gradual decline observed in this study likely reflects these cumulative microstructural processes.

Copyright © 2026| SSR-IIJLS by Society for Scientific Research under a CC BY-NC 4.0 International License 

doi: 10.21276/SSR-IIJLS.2026.12.1.38

The present study identified significant rightward hippocampal predominance across age groups. This aligns with prior structural MRI meta-analyses reporting mild but consistent right-sided asymmetry in healthy populations [5].

Structural asymmetry may reflect hemispheric functional specialization. The right hippocampus is more strongly associated with visuospatial processing, whereas the left is linked to verbal memory functions [9]. Importantly, asymmetry remained stable across age groups, suggesting that physiological lateralization persists despite global atrophic processes.

Recognition of normative asymmetry is clinically important, particularly when evaluating unilateral atrophy in temporal lobe epilepsy or early neurodegeneration.

Although males demonstrated slightly larger raw volumes, sex was not an independent predictor after regression adjustment. These findings are consistent with meta-analytic evidence indicating that hippocampal sexual dimorphism largely disappears after accounting for total brain size [10].

Tan *et al.* concluded that apparent sex differences in hippocampal volume are primarily attributable to global cranial size variation rather than region-specific effects [10]. The absence of age × sex interaction in the present study further suggests parallel aging trajectories between males and females.

Quadratic modeling demonstrated a small but significant nonlinear component, indicating accelerated decline in later decades. This supports prior longitudinal findings suggesting that hippocampal atrophy may intensify beyond midlife [1,11].

Jack *et al.* demonstrated measurable acceleration of whole-brain and medial temporal lobe atrophy in aging individuals followed longitudinally [8]. Although the present study is cross-sectional, nonlinear modeling strengthens biological plausibility.

Hippocampal atrophy is a validated biomarker for early Alzheimer's disease and mild cognitive impairment [12]. However, differentiation between normal aging and pathological decline requires age-stratified normative reference values.

Most normative databases derive from Western populations. Variations in cranial morphology, genetic background, and environmental factors may influence volumetric baselines [13]. The present study provides region-specific reference values for central India, which may enhance diagnostic precision in clinical radiology. Given the rising burden of dementia in India, the establishment of population-specific volumetric benchmarks is of increasing public health relevance.

**STRENGTHS**

- Balanced age stratification across three defined age groups.
- Detection of large effect sizes demonstrating strong age–volume association.
- Application of multivariate regression modeling.
- Evaluation of nonlinear (quadratic) aging trajectories
- Bilateral hippocampal assessment with asymmetry analysis.
- Comprehensive model diagnostics ensuring statistical robustness.

**LIMITATIONS**

- A cross-sectional study design limits causal inference.
- Absence of intracranial volume normalization.
- Single-center cohort, which may limit generalizability

Future longitudinal studies incorporating intracranial volume adjustment and hippocampal subfield segmentation would further enhance precision and improve characterization of aging trajectories.

**CONCLUSIONS**

This study demonstrates significant age-related hippocampal volume decline in a central Indian population, with an approximate reduction of 15 $mm^3$ per year and mild acceleration in later decades. Age accounts for more than half of volumetric variance, confirming hippocampal sensitivity to aging. Physiological rightward asymmetry persists across adulthood, and sex does not independently influence volumetric outcomes. The findings align with global literature while providing region-specific normative MRI data. These results enhance clinical differentiation between normal aging and pathological atrophy and support the development of population-specific neuroimaging reference databases. Future longitudinal, multicentric studies incorporating intracranial volume normalization and subfield analysis are warranted to refine aging trajectories further.

**CONTRIBUTION OF AUTHORS**

**Research concept-** P. Uday Kumar, Prof. Avantika Bamne

Copyright © 2026| SSR-IIJLS by Society for Scientific Research under a CC BY-NC 4.0 International License 

doi: 10.21276/SSR-IIJLS.2026.12.1.38

**Research design-** P. Uday Kumar, Prof. Avantika Bamne
**Supervision-** Prof. Avantika Bamne
**Materials-** P. Uday Kumar, Prof. Avantika Bamne
**Data collection-** P. Uday Kumar, Prof. Avantika Bamne
**Data analysis and interpretation-** Prof. Avantika Bamne
**Literature search-** P. Uday Kumar, Prof. Avantika Bamne
**Writing article-** P. Uday Kumar, Prof. Avantika Bamne
**Critical review-** Prof. Avantika Bamne
**Article editing-** P. Uday Kumar, Prof. Avantika Bamne
**Final approval-** Prof. Avantika Bamne

**REFERENCES**

[1] Fjell AM, Walhovd KB, Westlye LT, et al. When does brain aging accelerate? Dangers of quadratic fits in cross-sectional studies. Neuroimage, 2010; 50(4): 1376–83. doi: 10.1016/j.neuroimage.2010.01.061.

[2] Walhovd KB, Fjell AM, Reinvang I, et al. Effects of age on volumes of cortex, white matter and subcortical structures. Neurobiol Aging, 2005; 26(9): 1261–70. doi: 10.1016/j.neurobiolaging.2005.05.020.

[3] Burke SN, Barnes CA. Neural plasticity in the ageing brain. Nat Rev Neurosci., 2006; 7(1): 30–40. doi: 10.1038/nrn1809.

[4] Small SA, Schobel SA, Buxton RB, Witter MP, Barnes CA. A pathophysiological framework of hippocampal dysfunction in ageing and disease. Nat Rev Neurosci., 2011; 12(10): 585–601. doi: 10.1038/nrn3089.

[5] Shi F, Liu B, Zhou Y, Yu C, Jiang T. Hippocampal volume and asymmetry in healthy subjects: A meta-analysis of MRI studies. Hippocampus, 2009; 19(11): 1055–64. doi: 10.1002/hipo.20573.

[6] GBD 2019 Dementia Forecasting Collaborators. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: An analysis for the Global Burden of Disease Study 2019. Lancet Public Health, 2022; 7(2): e105–25. doi: 10.1016/S2468-2667(21)00249-8.

[7] India State-Level Disease Burden Initiative Mental Disorders Collaborators. The burden of mental disorders across the states of India: The Global Burden of Disease Study 1990–2017. Lancet Psychiatry, 2020; 7(2): 148–61. doi: 10.1016/S2215-0366(19)30475-4.

[8] Jack CR Knopman DS, Jagust WJ, Shaw LM, Aisen PS, et al. Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. Lancet Neurol., 2010; 9(1): 119–28. doi: 10.1016/S1474-4422(09)70299-6.

[9] Burgess N, Maguire EA, O'Keefe J. The human hippocampus and spatial and episodic memory. Neuron, 2002; 35(4): 625–41. doi: 10.1016/S0896-6273(02)00830-9.

[10] Tan A, Ma W, Vira A, Marwha D, Eliot L. The human hippocampus is not sexually-dimorphic: Meta-analysis of structural MRI volumes. Neuroimage, 2016; 124: 350–66. doi: 10.1016/j.neuroimage.2015.08.050.

[11] Scahill RI, Frost C, Jenkins R, Whitwell JL, Rossor MN, et al. A longitudinal study of brain volume changes in normal aging using serial registered magnetic resonance imaging. Arch Neurol., 2003; 60(7): 989-94. doi: 10.1001/archneur.60.7.989.

[12] Jack CR Jr, Petersen RC, Xu YC, Waring SC, O'Brien PC, et al. Medial temporal atrophy on MRI in normal aging and very mild Alzheimer's disease. Neurol., 1997; 49(3): 786–94. doi: 10.1212/WNL.49.3.786.

[13] Good CD, Johnsrude I, Ashburner J, Henson RN, Friston KJ, et al. Cerebral asymmetry and the effects of sex and handedness on brain structure. Neuroimage, 2001; 14(3): 685–700. doi: 10.1006/nimg.2001.0857.

**Open Access Policy:**
Authors/Contributors are responsible for originality, contents, correct references, and ethical issues. SSR-IIJLS publishes all articles under Creative Commons Attribution- Non-Commercial 4.0 International License (CC BY-NC). https://creativecommons.org/licenses/by-nc/4.0/legalcode