

# Association of stress and anxiety with Alzheimer's: post-COVID-19 pandemic global perspective

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## ABSTRACT

Alzheimer's is a neurodegenerative disorder mainly caused by aging, diabetes, stress, depression, anxiety, hypertension, obesity, etc. This bibliometric study investigated the correlation of stress and anxiety with Alzheimer's Disease to understand recent research trends and post-COVID-19 pandemic trending topics. The Web of Science database was utilized. The analysis was performed using the R package and VOSviewer software. A total of 305 articles were characterized and analyzed. The density visualization indicates that Alzheimer's disease and oxidative stress are the most prominent terms, followed by memory, dementia, anxiety, and stress. The most productive countries were China, the United States of America, and Iran.

**Key words:** Alzheimer's disease, Bibliometric study, Post-COVID-19, Stress and anxiety

## Dear Editor,

Alzheimer's Disease (AD) is a neurodegenerative disorder characterized by cognitive decline, memory impairment, and neuropathological changes accompanied by neuropsychiatric symptoms. AD typically begins gradually and progressively leads to 60-70% of dementia cases<sup>1</sup>. It is caused by factors such as aging, diabetes, stress, depression, anxiety, hypertension, obesity, smoking, traumatic brain injury, air pollution, excessive alcohol consumption, hearing impairment, and limited social contact<sup>2</sup>. According to the vicious cycle of stress (**Figure 1 A**), the right arc of the cycle shows that elevated stress leads to AD through the rapid development of pathology and loss of cognitive functions. Conversely, the left arc indicates that the disease perturbs stress-responsive neural circuits, producing neuropsychiatric symptoms like stress, anxiety, and aggressive behavior. The central part involves the hypothalamic Corticotrophin Releasing Factor (CRF), which activates the Pituitary Adrenocorticotrophic Hormone (ACTH) and releases cortisol from the adrenal cortex, playing a vital role in the exacerbation of AD by stress leading to ongoing neurodegeneration<sup>1</sup>. This bibliometric study investigates the correlation between stress and anxiety with AD to understand recent research trends and plot the global scientific production in the post-coronavirus disease 2019 (COVID-19) pandemic era. Bibliometric analysis uniquely summarizes the cross-disciplinary quantitative process and accesses multi-

ple sources of knowledge using mathematical and statistical techniques in a single domain.

The Web of Science Core Collection database (WoSCC) was utilized for the integrative analysis of literature published during the post-COVID-19 pandemic (2020-2023). The analysis was performed using VOSviewer software, an online bibliometric tool (<http://bibliometric.com/>), and Biblioshiny, an R package tool. The potential key terms used were "stress" OR "anxiety" AND "Alzheimer's Disease" in the title. The dataset was downloaded in both plaintext and tab-delimited formats. The search was limited to publication years (2020-2023), language (English), and document type (research article). In total, only 305 articles were characterized and plotted. These articles were written by 1,938 authors and published in 184 journals.

The results (**Figure 1B**) show that the density visualization indicates that Alzheimer's disease and oxidative stress are the most prominent terms, followed by memory, dementia, anxiety, and stress. To better understand the relationship between different topics in the stress and anxiety association with AD, an unsupervised machine learning model was applied. The Multiple Correspondence Analysis (MCA) method was used. The model generates two clusters: a red cluster and a blue cluster, as presented in **Figure 1C**. The red cluster is more focused on anxiety, stress, depression, diseases, memory, expression, cognitive, oxidative, effect, and brain. The blue cluster is focused on Alzheimer. (**Figure 1 D**) indicates inter-country collaboration. The most productive country

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## History

- Received: Aug 07, 2024
- Accepted: Sep 23, 2024
- Published Online: Sep 30, 2024

DOI : 10.15419/bmrat.v11i9.915

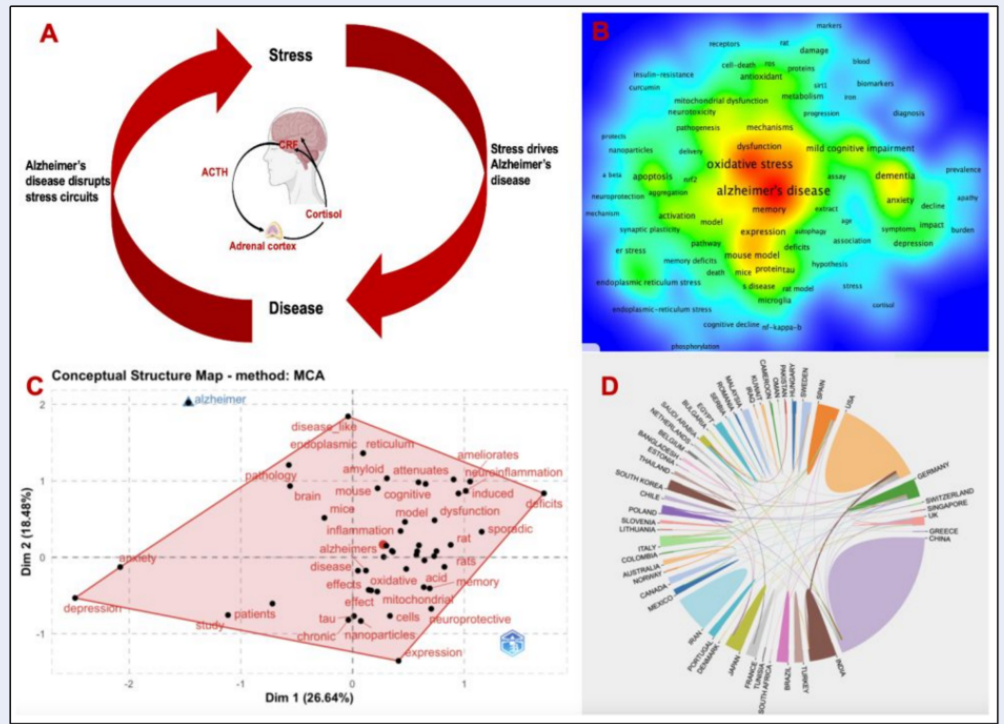


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**Cite this article :** Khan M, Ahmad T. Association of stress and anxiety with Alzheimer's: post-COVID-19 pandemic global perspective. *Biomed. Res. Ther.* 2024; 11(9):6720-6722.



**Figure 1:** A. Mechanism of stress leading to the AD; B: Density visualization map; C: Conceptual structure map; D: Research collaboration among different countries.

was China, followed by the United States of America (USA) and Iran. China has strongly collaborated with the United Kingdom, Italy, and Spain, while the USA has strong collaboration with India and Canada. Analysis of the titles shows that, besides the search key terms, other trending topics are disease, oxidative, model, pathology, mitochondrial, patient, brain, neuronal, and antioxidant. It is worth exploring and understanding the causes of neurodegenerative diseases and dementia to search for remedies and save the aged population from experiencing extensive dementia.

**ABBREVIATIONS**

ACTH: Adrenocorticotrophic Hormone, AD: Alzheimer’s Disease, COVID-19: Coronavirus disease 2019, CRF: Corticotrophin Releasing Factor, MCA: Multiple Correspondence Analysis, USA: United States of America, WoSCC: Web of Science Core Collection database

**ACKNOWLEDGMENTS**

We acknowledge our respective universities. We also want to acknowledge the developers of bibliometric online tool, VOSviewer software and R package.

**AUTHOR’S CONTRIBUTIONS**

Both the authors equally contributed to the study design, methodology, data collection, analysis, writing and editing. The authors read and approved the final version for publication.

**FUNDING**

None.

**AVAILABILITY OF DATA AND MATERIALS**

All the data and findings are presented in the study. The coded data will be made available on a reasonable request to the corresponding author.

**ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

Not applicable.

**CONSENT FOR PUBLICATION**

Not applicable.

**COMPETING INTERESTS**

The authors declare that they have no competing interests.

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