



## Herpes zoster and Alzheimer's disease

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Dear Editor,

One retrospective cohort study conducted by Bae et al. published in *European Archives of Psychiatry and Clinical Neuroscience* revealed that people with herpes zoster had a higher hazard for Alzheimer's disease compared to people without herpes zoster in Korea (adjusted hazard ratio = 1.11 and 95% confidence interval 1.04–1.19) [1]. To the contrary, one case–control study in Korea revealed no association between Alzheimer's disease and herpes zoster (adjusted odds ratio 0.91, 95% confidence interval 0.83–1.00 in the group aged < 80 years, and adjusted odds ratio 0.88, 95% confidence interval 0.78–1.00 in the group aged ≥ 80 years) [2]. Both studies used the same dataset from the Korean National Health Insurance Service (NHIS), but conflicting results were noticed. Some points should be discussed.

First, when the host's specific cell-mediated immunity is declined, herpes zoster may develop due to the reactivation of latent varicella-zoster virus in dorsal root ganglia. The major manifestation of herpes zoster is in the skin, not in the brain. In addition, amyloid plaques and neurofibrillary tangles are two hallmarks for Alzheimer's disease [4]. But no study examines the association of varicella-zoster virus with amyloid plaques and neurofibrillary tangles. The higher hazard of Alzheimer's disease found in Bae et al. study could be due to surveillance bias. That is, people with herpes zoster needed to frequently visit clinicians because

of the post-herpetic neuralgia. So people with post-herpetic neuralgia were more likely to be diagnosed with Alzheimer's disease. Similarly, people with herpes zoster who took antiviral therapy were less likely to suffer from post-herpetic neuralgia [3]. Herpes zoster people on antiviral therapy did not need to frequently visit clinicians, so the probability that these treated people were diagnosed with Alzheimer's disease could be lower compared to those without taking antiviral therapy. Second, based on Bae et al. study [1], the incidences of dementia were 8.53 per 1000 person-years in the herpes zoster group and 4.39 per 1000 person-years in the non-herpes zoster group. We estimated that the absence of herpes zoster might reduce about four cases of dementia per 1000 person-years of follow-up. This will not happen in real world because no definite evidence proves that herpes zoster is a risk factor for dementia. Also, no definite evidence proves that vaccination for herpes zoster may reduce the risk of dementia. We agree with the authors' conclusion that the biological mechanisms of the association between herpes zoster and dementia should be further investigated.

### Declarations

**Conflict of interest** The authors disclose no conflicts of interest.

### References

1. Bae S, Yun SC, Kim MC, Yoon W, Lim JS, Lee SO, Choi SH, Kim YS, Woo JH, Kim SY, Kim SH (2020) Association of herpes zoster with dementia and effect of antiviral therapy on dementia: A population-based cohort study. *Eur Arch Psychiatry Clin Neurosci*
2. Choi HG, Park BJ, Lim JS, Sim SY, Jung YJ, Lee SW (2021) Herpes zoster does not increase the risk of neurodegenerative dementia: a case-control study. *Am J Alzheimers Dis Other Dement*. <https://doi.org/10.1177/15333175211006504>
3. Sra KK, Tyring SK (2004) Treatment of postherpetic neuralgia. *Skin Therapy Lett* 9:1–4
4. Weller J, Budson A (2018) Current understanding of Alzheimer's disease diagnosis and treatment. *F1000Res* 7:F1000

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