Mid life modifiable risk factors for late life Alzheimer's disease

Sir,

The article on cross-sectional study on thyroid status in North Indian elderly outpatients with dementia has brought into prominence the much encountered geriatric condition and its association with subclinical hyperthyroidism.[1] A treatable cause like low thyroid stimulating hormone with normal T3, T4 is thus a useful predictor of Alzheimer's disease (AD) and dementia in old age. There have been several studies on the possible predisposing factors, which can forecast the onset of dementia, in the presymptomatic stage. In this letter, we would touch upon some of the early onset risk factors, apart from hyperthyroidism, which can be modified for primary prevention of AD.

Vascular risk factors leading to an increase in prevalence of vascular cognitive impairment and vascular dementia is well-documented, while pathogenesis of AD is still an area of vast research. Vascular risk factors causing an increase in AD have also been suggested. Some cross-sectional studies exist associating systolic hypertension and hypercholesterolemia with AD. However, since cross-sectional studies cannot readily determine causality, the results have been conflicting. On the contrary, a few large population-based, longitudinal studies have been performed, one conducted in a Swedish elderly population aged 70 years, followed up for 9-15 years by Skoog *et al*., and the other a 25 year follow-up in Japanese-American men with a mean age of 53 by Launer *et al*.[2,3] Both these studies implicated midlife hypertension as predisposing to AD. Additionally, Finnish men aged 70-89 with AD were found to have had hypercholesterolemia about 15-25 years prior to the onset of the disease. A study in a Finnish population after an average of 21 years of follow-up showed that the coexistence of both these risk factors further increased the risk of AD. These studies suggested that apart from inducing atherosclerosis, reduced cerebral blood flow, and ischemia in strategic cortical or subcortical lobe necessary for cognitive impairment like angular gyrus, thalamus, frontal or temporal lobe, both hypertension and atherosclerosis can themselves directly cause neurodegeneration of AD.[4]

Body mass index is an inexpensive and easily performed assessment of one's nutritional status and is a valuable indicator for the risk of dementia. Kivipelto *et al*.,[5] opined that midlife obesity was a significant risk factor for late life dementia and AD. Obesity, an essential component of metabolic syndrome which includes hypertension, diabetes mellitus, insulin resistance, and dyslipidemia, may contribute to cognitive impairment due to clustering with other vascular risk factors. However, even in the absence of other variables, especially diabetes mellitus, there was a consistent association between a BMI more than 30 and dementia in late life.

AD is one of the leading causes of irreversible cognitive decline in late life and age is the greatest risk factor. Therefore, any intervention causing a delay in onset, even slightly, could have an enormous impact on geriatric health. Since obesity, hypertension, and hypercholesterolemia in midlife can all be treated, timely interventions could be a step toward prevention of AD.

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