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# Alcohol, Circadian Glymphatic Dysfunction, and Neurodegenerative Protein Accumulation: An Emerging Concern in the Indian Context

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***Abstract***

*Alcohol consumption has long been identified as a major public health issue, yet its deeper and more subtle effects on the human brain are only now coming into sharper focus. Traditional explanations often emphasize direct neuronal damage, but emerging research in neuroscience suggests a more intricate story. Recent findings indicate that alcohol not only harms brain cells but also disrupts the body's internal biological clock – the circadian rhythm – which plays a critical role in regulating sleep, hormonal balance, and metabolic processes. When this natural rhythm becomes disturbed, it can interfere with the brain's glymphatic system, a specialized "cleaning network" responsible for flushing out toxic waste products during sleep. This glymphatic pathway is essential for clearing harmful proteins such as amyloid-β and tau. When these proteins accumulate, they can contribute to the development and progression of neurodegenerative conditions, including Alzheimer's disease and other forms of dementia. The hypothesis explored in this paper proposes that alcohol-induced circadian disruption reduces the efficiency of glymphatic clearance, allowing neurotoxic proteins to build up over time and accelerating cognitive decline. Within the Indian context, this issue becomes particularly relevant. Rapid urbanization, hectic work schedules, late-night social drinking, and widespread sleep deprivation are increasingly common lifestyle patterns. These changes coincide with a noticeable rise in dementia cases across the country. A realistic case study from India further illustrates how chronic alcohol use combined with irregular sleep habits can gradually impair brain health, highlighting the urgent need for greater awareness and preventive interventions.*

**Keywords:** Alcohol consumption, cerebrospinal fluid, dementia, glymphatic pathway, plasma biomarkers

## INTRODUCTION

In India, alcohol holds a complex place within society – woven into celebrations, cultural traditions, social gatherings, and even stress-coping behaviors. While the visible social aspects of drinking often dominate public attention, the biological consequences remain far less recognized. Data from the National Family Health Survey (NFHS-5, 2019–21) show that 22.4% of Indian men and 0.7% of women aged 15–49 consume alcohol, with certain states, such as Goa (59%) and Arunachal Pradesh (53%), reporting particularly high prevalence. These statistics highlight not only regional variations but also the embedded nature of alcohol use within different communities across the country [1].

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At the same time, India is experiencing a significant rise in cognitive decline and dementia-related disorders. Currently, an estimated 8.8 million Indians live with dementia, and projections indicate that this number may exceed 11 million by 2030. Often, discussions surrounding alcohol emphasize addiction, liver cirrhosis, accidents, and social harms. However, what receives far less

 

scrutiny is alcohol's impact on the brain – especially its subtle interference with circadian rhythms, sleep quality, and long-term neurological Emerging neuroscience shows that alcohol does more than cause direct neuronal injury. It disrupts the body's natural 24-hour clock, which regulates sleep–wake cycles, hormone secretion, and cellular repair. When circadian rhythms are disturbed, sleep becomes fragmented and shallow. This poses a deeper problem: the brain performs most of its "cleaning functions" during high-quality sleep through the glymphatic system, a specialized pathway responsible for clearing toxins, including amyloid-β and tau proteins.

If alcohol consumption leads to poor or irregular sleep – something increasingly common among Indians due to nightlife patterns, shift work, stress, and late-evening drinking – the glymphatic system may fail to function efficiently [2]. Over time, this could allow neurotoxic waste products to accumulate, contributing to earlier or faster cognitive decline. This link between alcohol, disrupted circadian biology, and impaired brain clearance mechanisms is still underexplored in India but may play an important role in understanding the country's rising dementia burden.

As India continues to modernize, adopting lifestyle patterns that compromise sleep health, the neurological impact of alcohol deserves deeper research and stronger public awareness. Recognizing this connection early could open new avenues for prevention and healthier policy interventions in the years ahead.

## THE BRAIN'S NIGHTLY CLEANING SYSTEM

The glymphatic system functions as the brain's own internal housekeeping network, working silently and continuously to maintain neural health. Its activity peaks during deep, restorative sleep, when the brain's cells naturally shrink to create wider channels for cerebrospinal fluid (CSF) to circulate. This fluid washes through brain tissue, clearing metabolic waste products, including amyloid-β and tau proteins – substances strongly associated with Alzheimer's disease and other neurodegenerative conditions. Importantly, this cleansing process is tightly regulated by the body's circadian clock, meaning it follows a daily rhythm and is most effective during the night [3].

When an individual's sleep becomes delayed, irregular, or frequently interrupted – as commonly seen in people who consume alcohol late into the evening – the timing and quality of glymphatic activity are disrupted. Alcohol can interfere with both the depth of sleep and the ability to enter slow-wave sleep, the stage where the glymphatic system is most active. Over prolonged periods, reduced clearance of harmful proteins may lead to their gradual accumulation within the brain [4]. This build-up can create an environment that promotes inflammation, neuronal stress, and ultimately the early stages of neurodegeneration. Understanding this connection highlights why maintaining healthy sleep patterns is essential for long-term brain function, particularly in populations with high rates of night-time drinking.

## HOW ALCOHOL DISRUPTS THE BODY CLOCK

Alcohol interferes with the body's master clock – the circadian system – in several interconnected ways. One of the most immediate effects is the suppression of melatonin, the hormone responsible for signaling the brain that it is time to sleep. When melatonin levels drop, falling asleep becomes more difficult, and the natural timing of the sleep–wake cycle begins to shift. Beyond this, alcohol influences the activity of core circadian genes that regulate daily physiological functions, including metabolism, hormone release, and cellular repair. Disrupting these genes can throw multiple body systems out of sync, creating a ripple effect that extends far beyond sleep.

Perhaps most importantly, alcohol fragments slow-wave sleep, the deep stage of sleep when the glymphatic system is most active [5]. This is the period during which the brain clears out accumulated toxins and metabolic by-products. Even moderate drinking in the evening can reduce the amount of slow-wave sleep obtained, meaning that the brain gets fewer opportunities to perform its nightly maintenance. Over time, this disruption may impair glymphatic clearance and contribute to the gradual build-up of harmful proteins.

 

In many Indian cities, these biological effects are magnified by lifestyle patterns. Growing nightlife cultures, long work hours, and rising stress levels have made evening or post-dinner drinking increasingly common. While often seen as a way to unwind, this habit may be pushing sleep timing later and creating chronic circadian misalignment. Although rarely measured or discussed, this misalignment carries significant physiological consequences. Understanding these subtle but impactful interactions between alcohol, daily rhythms, and brain health is essential for addressing India's evolving public health challenges.

## WHEN GLYMPHATIC FLOW FALTERS

Alcohol compromises the function of aquaporin-4 (AQP4) channels on astrocytes that regulate brain fluid movement. Chronic alcohol use can cause these channels to lose polarity, reducing CSF flow and slowing brain waste clearance. Over years, this impaired glymphatic activity could create a toxic buildup of amyloid-β and tau – proteins that underlie Alzheimer's and other dementias [6]. Despite growing dementia rates in India, no Indian research has yet examined this glymphatic pathway, making it an open field for discovery.

## A CASE STUDY: THE 47-YEAR-OLD ENGINEER

Ramesh Verma, a 47-year-old software engineer from Pune, began drinking socially in his late twenties. Over time, his habit evolved into nightly consumption – usually 2–3 pegs of whiskey after 10 p.m. He often slept around 1–2 a.m., waking early for work. He complained of "mental fog," morning fatigue, and forgetfulness. By age 45, he began missing project deadlines and forgetting client details – unusual for his once sharp mind. Medical evaluation showed normal liver function and only mild hypertension. However, sleep monitoring revealed severe fragmentation and suppressed melatonin rhythm. MRI scans suggested reduced perivascular fluid movement, an indirect marker of glymphatic inefficiency. Neurocognitive testing found subtle deficits in working memory and attention – early signs of mild cognitive impairment [7]. Ramesh's pattern of nighttime alcohol intake, combined with chronic circadian disruption, likely impaired his glymphatic function, setting in motion a slow decline. After quitting alcohol and undergoing sleep therapy, his symptoms stabilized but did not fully reverse.

## THE INDIAN PICTURE: DATA AND LIFESTYLE TRENDS

NFHS-5 data indicate national consumption of 22.4% among men, but much higher in certain states. Late-night drinking is increasingly common in urban professionals, especially in IT and corporate sectors.

The Longitudinal Ageing Study in India (LASI, 2017–18) found 12–13% prevalence of sleep disorders among adults over 60. India has 8.8 million dementia cases, with projections exceeding 11 million by 2030. Hypertension (220 million adults) and diabetes (101 million) compound risks of vascular and neurodegenerative brain injury. Doctors at tertiary centers, like AIIMS, report a rise in young stroke and cognitive decline cases, some linked to alcohol and erratic sleep schedules [8].

## HYPOTHESIS

Chronic alcohol consumption, particularly during night hours, disrupts circadian rhythms and glymphatic activity, leading to reduced clearance of neurotoxic proteins and early cognitive decline.

## PROPOSED STUDY FRAMEWORK

- *Participants:* Adults aged 30–60 years, grouped by drinking patterns (none, moderate/daytime, heavy/nighttime).

### Methods

- MRI using DTI-ALPS index for glymphatic function.
- Actigraphy and melatonin sampling for circadian rhythm profiling.
- Plasma biomarkers (amyloid-β, tau).
- Cognitive and sleep assessments.

 

- *Expected Findings:* Night-time drinkers will exhibit lower melatonin amplitude, reduced glymphatic indices, and higher neurodegenerative biomarkers [9].

## IMPLICATIONS FOR INDIA

If proven, these findings could shift India's health policies from focusing purely on alcohol quantity to also considering timing. Public awareness campaigns might emphasize how late-night alcohol can quietly affect brain health decades before symptoms appear. Programs, like Ayushman Bharat and Nasha Mukt Bharat Abhiyaan, could integrate sleep and circadian education, helping people recognize early cognitive risks.

## CHALLENGES AND FUTURE WORK

India lacks imaging infrastructure to routinely measure glymphatic flow. Social stigma around alcohol may limit participant honesty. Long-term studies will be needed to link early biomarkers to later disease outcomes.

Yet, exploring this path can open doors for preventive neurology in India – a field that could reduce dementia onset by years if risks are addressed early [10].

## CONCLUSION

Ramesh Verma's case represents many silent stories unfolding across Indian cities – people who function well outwardly but slowly lose mental sharpness due to lifestyle rhythms misaligned with biology. Alcohol, once considered harmful mainly to the liver, might also be impairing the brain's natural self-cleaning rhythm. Recognizing this invisible link between when we drink, how we sleep, and how our brain clears waste could change the way India approaches brain health in the 21st century.

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