ECM 2025 Conference
The 3rd International Electronic Conference on Microbiology
01–03 April 2025 | Online
MDPI

HHV-6 in Liver Damage: Innocent Presence or Active Player in Alcohol-Induced Injury?

Anda Upane[1], Simons Svirskis[2], Sandra Skuja[1]
[1]Joint Laboratory of Electron Microscopy, Institute of Anatomy and Anthropology, Riga Stradins University, Riga, Latvia
[2]Institute of Microbiology and Virology, Riga Stradins University, Riga, Latvia

INTRODUCTION & AIM

Human herpesvirus 6 (HHV-6), a widely distributed member of the *Herpesviridae* family, establishes lifelong latency in monocytes and macrophages. The persistence of HHV-6 under immunosuppressive conditions, such as chronic alcohol consumption, may potentiate liver inflammation and exacerbate tissue damage by synergising with the hepatotoxic effects of ethanol (1). This interaction could raise significant concerns in the context of infectious diseases, as it poses a heightened risk to individuals with a history of heavy alcohol use, particularly those with underlying comorbidities or compromised immune function.
Nuclear factor kappa B (NF-κB), a transcription factor essential for transactivating target genes involved in immune and inflammatory responses, and CD163, expressed on anti-inflammatory macrophages, provide valuable insights into tissue damage during the presence of HHV-6 infection (2, 3).

RESULTS & DISCUSSION

HHV-6-positive liver lobules were identified in 64% of the controls, 79% of young alcohol users and 75% of chronic alcohol users (Figure 1).
The total CD163-positive cell count in the lobules increased significantly in the young alcohol user group (p = 0.1256) and the chronic alcohol user group (p = 0.0157) compared to the controls (Figure 2).
NF-κB expression intensity in the lobular area was significantly higher in young alcohol users (p < 0.005), and both intensity and distribution were notably increased in the chronic alcohol user group (p < 0.001 and p = 0.02, respectively) compared to the controls.

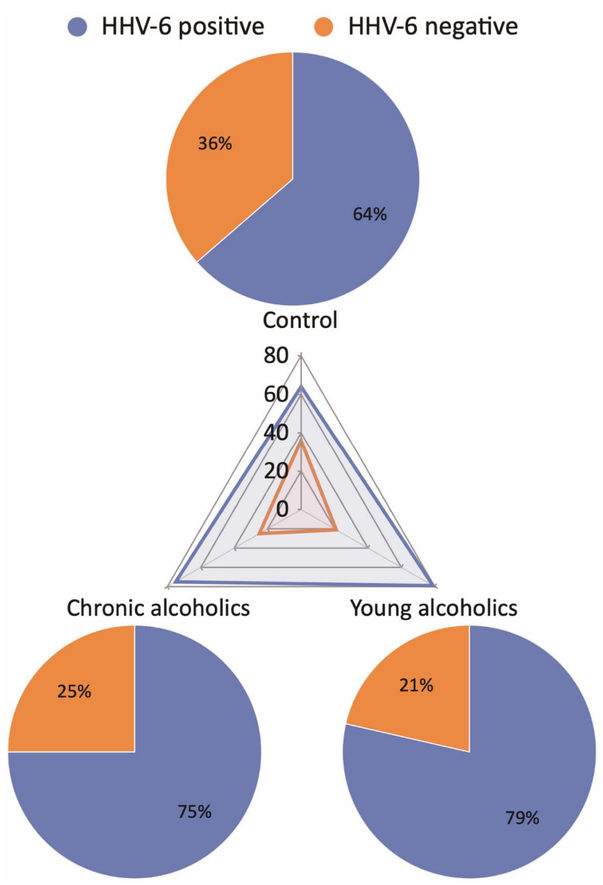

Figure 1. *Proportion of HHV-6-positive and HHV-6-negative liver lobules in control, young alcohol and chronic alcohol user groups.*

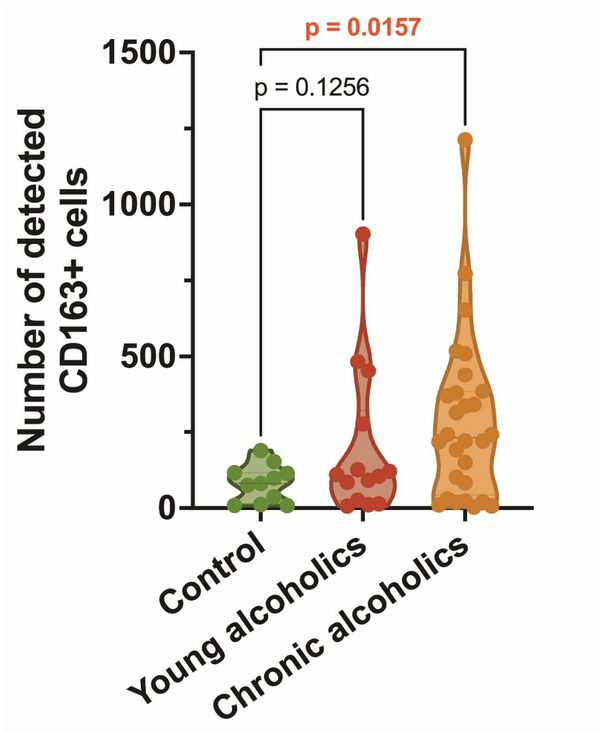

Figure 2. *CD163-positive cell counts across study groups.*

There was also a strong correlation between NF-κB expression intensity and distribution and HHV-6-positive cells in the central vein area in the age-matched group (p = 0.006 and p = 0.034, respectively), as well as a correlation between HHV-6-positive cells in the lobular area and CD163 expression in the portal area (p = 0.039).

METHOD

Fifty-four liver tissue specimens were collected from the following groups:
- control (n = 11)
- young alcohol user group (age-matched group) (n = 15)
- chronic alcohol user group (n = 28).

Specimens were immunohistochemically stained with anti-CD163 (Figure 3), anti-NF-κB (Figure 4) and anti-HHV-6 antibodies (Figure 5) and analysed via light microscopy. HHV-6- and CD163-positive cells were counted quantitatively, while both the intensity and distribution of NF-κB expression were analysed semi-quantitatively.
Statistical analysis was performed using SPSS 28.0 and GraphPad Prism 9.0.

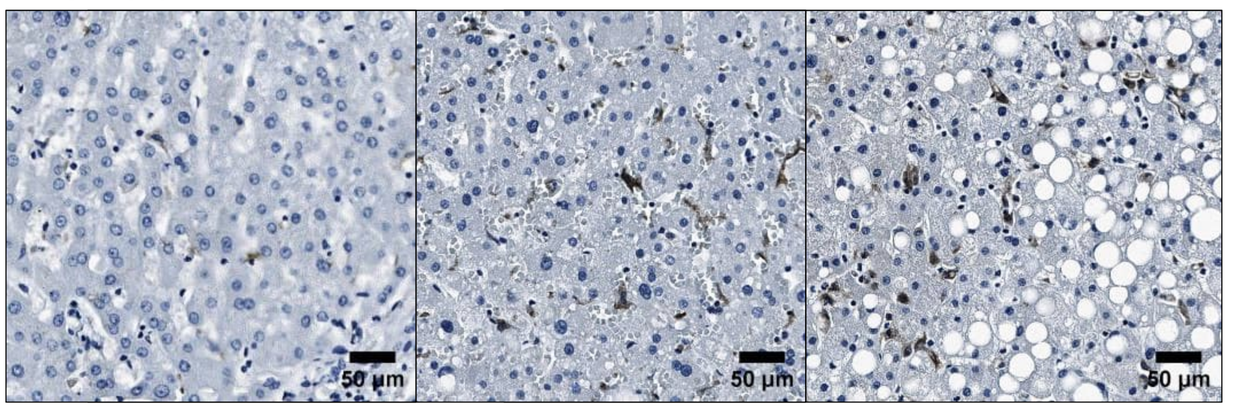

Figure 3. *CD163 expression – control, young-alcohol users, chronic alcohol users.*

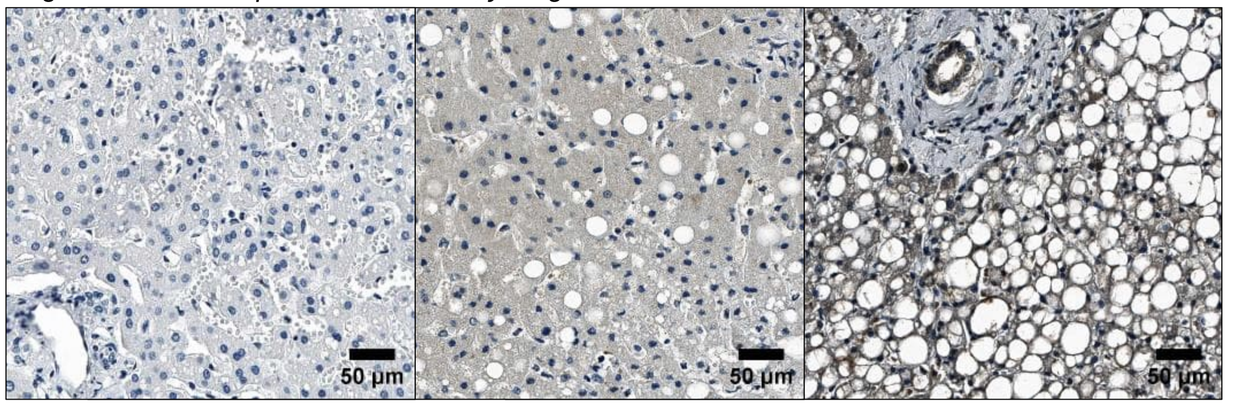

Figure 4. *NF-κB expression – control, young-alcohol users, chronic alcohol users.*

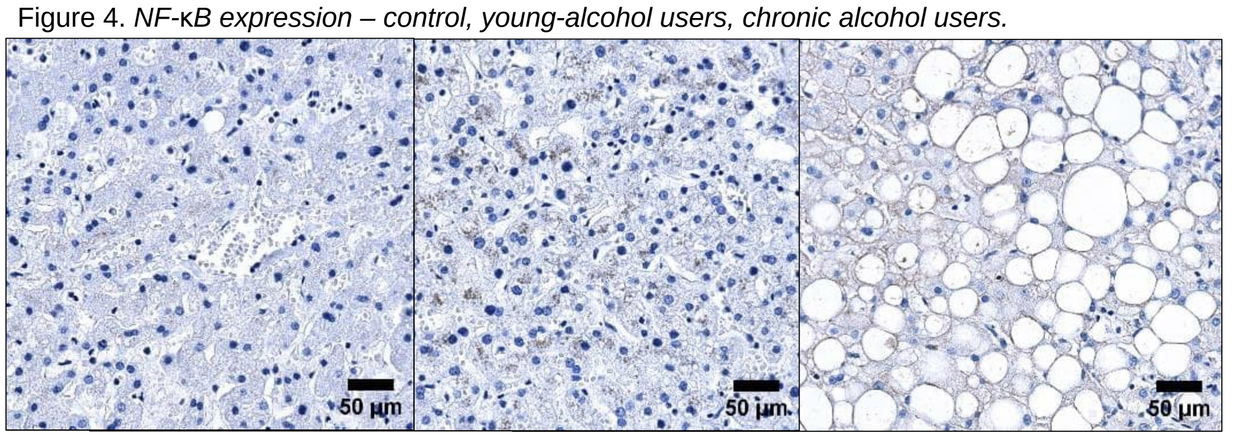

Figure 5. *HHV-6 expression – control, young-alcohol users, chronic alcohol users.*

CONCLUSION

Chronic alcohol consumption increases liver inflammation and damage, potentially exacerbated by HHV-6 persistence. Further studies are needed to confirm these interactions and explore the mechanisms driving the synergistic effects of HHV-6 and ethanol on liver tissue damage.

REFERENCES

1. Phan, T. L., Lautenschlager, I., Razonable, R. R., & Munoz, F. M. (2018). HHV-6 in liver transplantation: A literature review. *Liver international : official journal of the International Association for the Study of the Liver*, 38(2), 210–223. https://doi.org/10.1111/liv.13506
2. Nowak, A. J., & Relja, B. (2020). The Impact of Acute or Chronic Alcohol Intake on the NF-κB Signaling Pathway in Alcohol-Related Liver Disease. *International journal of molecular sciences*, 21(24), 9407. https://doi.org/10.3390/ijms21249407
3. Malherbe, D. C., & Messaoudi, I. (2022). Transcriptional and Epigenetic Regulation of Monocyte and Macrophage Dysfunction by Chronic Alcohol Consumption. *Frontiers in immunology*, 13, 911951. https://doi.org/10.3389/fimmu.2022.911951