

Patients with hepatitis B infection twice as likely to develop non-Hodgkin lymphoma

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A South Korean study has shown that patients infected with hepatitis B (HBV) are around twice as likely to develop a common form of non-Hodgkin lymphoma (NHL). This is the conclusion of an Article published Online First in *The Lancet Oncology*, written by Dr Eric Engels, National Cancer Institute, Rockville, MD, USA, and Prof Sun Ha Jee, Graduate School of Public Health, Yonsei University, Seoul, South Korea, and colleagues.

NHL is a cancer of the blood. Several studies have already established a causal link between [hepatitis C](#) (HCV) infection and increased risk of NHL, but studies on [hepatitis B](#) and NHL have so far been small. The link to NHL for both HBV and HCV is thought to involve chronic immune stimulation in the setting of sustained liver infection. Sustained immune activation may lead lymphocytes to develop [DNA mutations](#) that can promote their proliferation and progression to NHL.

HBV infection was endemic in South Korea until 1995, when universal HBV vaccination of neonates was implemented. Before the introduction of vaccination, about 7% of South Korean adults had detectable plasma concentrations of hepatitis B surface antigen (HBsAg), which is consistent with chronic HBV infection. HBV infection remains common in South Korean adults, despite the availability of neonatal vaccination, because of infections acquired in childhood during previous years. In this study, the authors assessed the association between [chronic HBV infection](#) and subsequent development of NHL in a South Korean cohort.

Using data from The Korean Cancer Prevention Study, the researchers showed that 53 045 (9%) of 603 585 participants tested positive for hepatitis B at baseline. Subsequently, 133 hepatitis-B positive (HBV+) and 905 hepatitis-B negative (HBV-) individuals developed NHL. HBV+ participants had an increased risk of NHL overall compared with those who were HBV- (incidence 19.4 vs 12.3 per

100 000 person-years; translating to almost double the risk of NHL for HBV+ individuals). NHL risk was increased consistently throughout 14 years of follow-up

Increased risk was also recorded for malignant immunoproliferation, a constellation of immune disorders related to NHL. HBV+ persons were almost four times as likely to develop this rare condition. Hepatitis-B positivity was not associated with follicular or T-cell NHL, Hodgkin's lymphoma, multiple myeloma, or various leukaemias.

The authors conclude: "In this large cohort study of healthy workers and their families in South Korea, we documented an excess risk of NHL in people infected with HBV...Additional research is needed to clarify whether the association between HBV infection and NHL is causal."

They conclude: "For HCV-infected patients with low-grade NHL (especially marginal zone lymphomas), HCV treatment seems effective for haematological remission. Thus, we speculate that treatment directed at HBV in similar low-grade NHLs might lead to a clinical response and remove the need for chemotherapy. Further investigation in appropriate clinical series will be important."

In a linked Comment, Dr Sook-Hyang Jeong, Seoul National University, Bundang Hospital, South Korea, says: "If the association is causal, might the globally increasing implementation of universal HBV vaccination and increasing use of antiviral drugs for treatment of chronic HBV-related liver disease reduce development of NHL? Engels and colleagues commented that the causal association is small in magnitude, and that HBV infection would account for only a few NHL cases. Thus, those efforts would be expected to have a limited effect on NHL incidence."

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