Chronic hepatitis B associates with an increased risk of B cell non-Hodgkin's lymphoma and multiple myeloma

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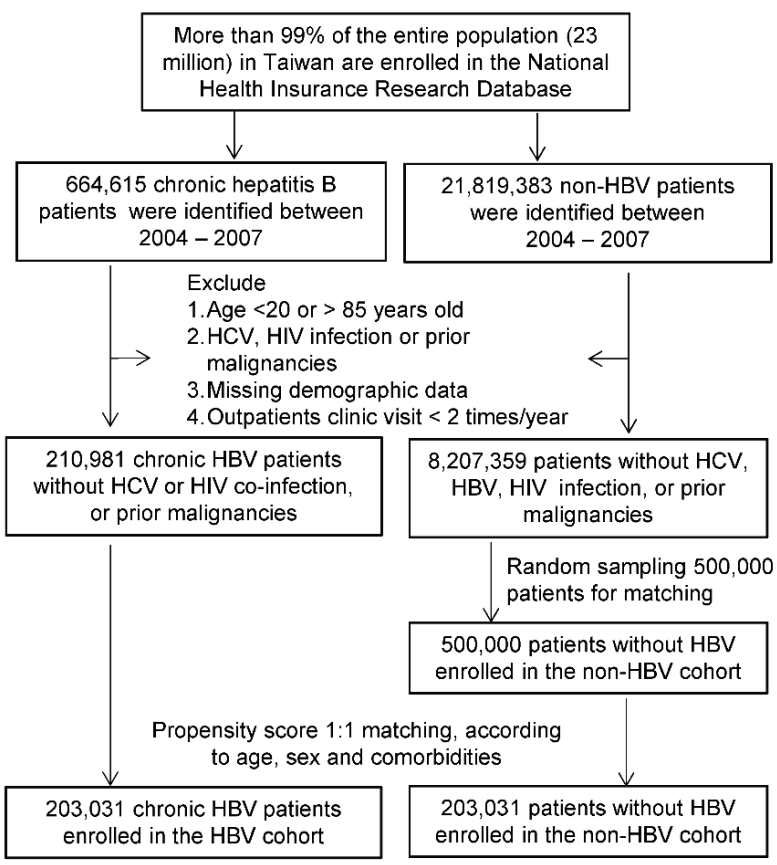
Objectives: Whether chronic hepatitis B links to lymphoma development remains controversial. We aimed to investigate the association between chronic hepatitis B and lymphoma and its subtypes using a nationwide population-based cohort.

Methods: Patients with the diagnosis of chronic hepatitis B were retrieved from the Taiwan National Health Insurance Research Database during 2004-2007. Those with prior malignancies, co-infected with hepatitis C or human immunodeficiency virus, or without regular follow-up were excluded. The age, sex, comorbidities, and medical visits of the HBV cohort were matched by propensity scores to another non-HBV cohort. Both cohorts were followed longitudinally until 2012 for a new diagnosis of lymphoma.

Results: Overall, 203,031 patients in the respective HBV and non-HBV cohorts were included with a mean follow-up of 7 and 9 years, respectively. The lymphoma incidence rate was significantly higher in the HBV cohort than in the non-HBV cohort (29.4 vs. 15.9 per 100,000 person-years, P<0.0001). After adjustment for comorbidities and medical visits, HBV infection was an independent risk factor associated with lymphoma (HR: 2.23, 95%CI: 1.91-2.62, P<0.0001) and NHL (HR: 2.35, 95%CI: 1.94-2.84, P<0.0001) development, and specifically, increased the risk of diffuse large B cell lymphoma (HR: 2.84, 95%CI: 2.16-3.73, P<0.0001), other B cell lymphoma (HR: 3.33, 95%CI: 2.03-5.48, P<0.0001), and multiple myeloma (HR: 1.67, 95%CI: 1.11-2.51, P=0.014). The association remains significant even if we excluded lymphoma development within the first year.

Figure 1. Flowchart of cohort selection in this study



Conclusions: Chronic Hepatitis B is temporally associated with a 2.23-fold increased risk of lymphoma, especially B-cell NHL and multiple myeloma.

Figure 2. Cumulative risk of HBV infection in (A) all lymphoma, and (B) NHL development

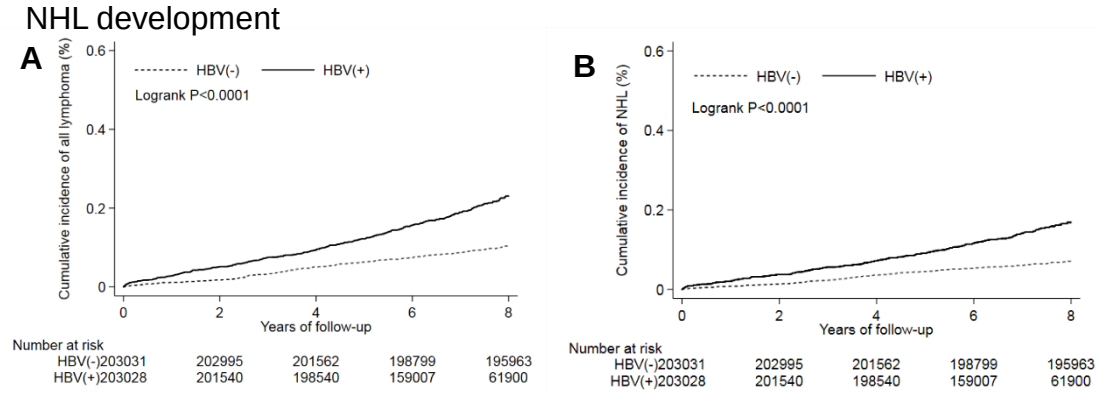


Figure 3. Cumulative risk of HBV infection in (A) diffuse large B cell lymphoma, (B) marginal zone lymphoma, (C) other B cell NHL, (D) other T cell NHL, (E) Hodgkin's lymphoma, (F) multiple myeloma

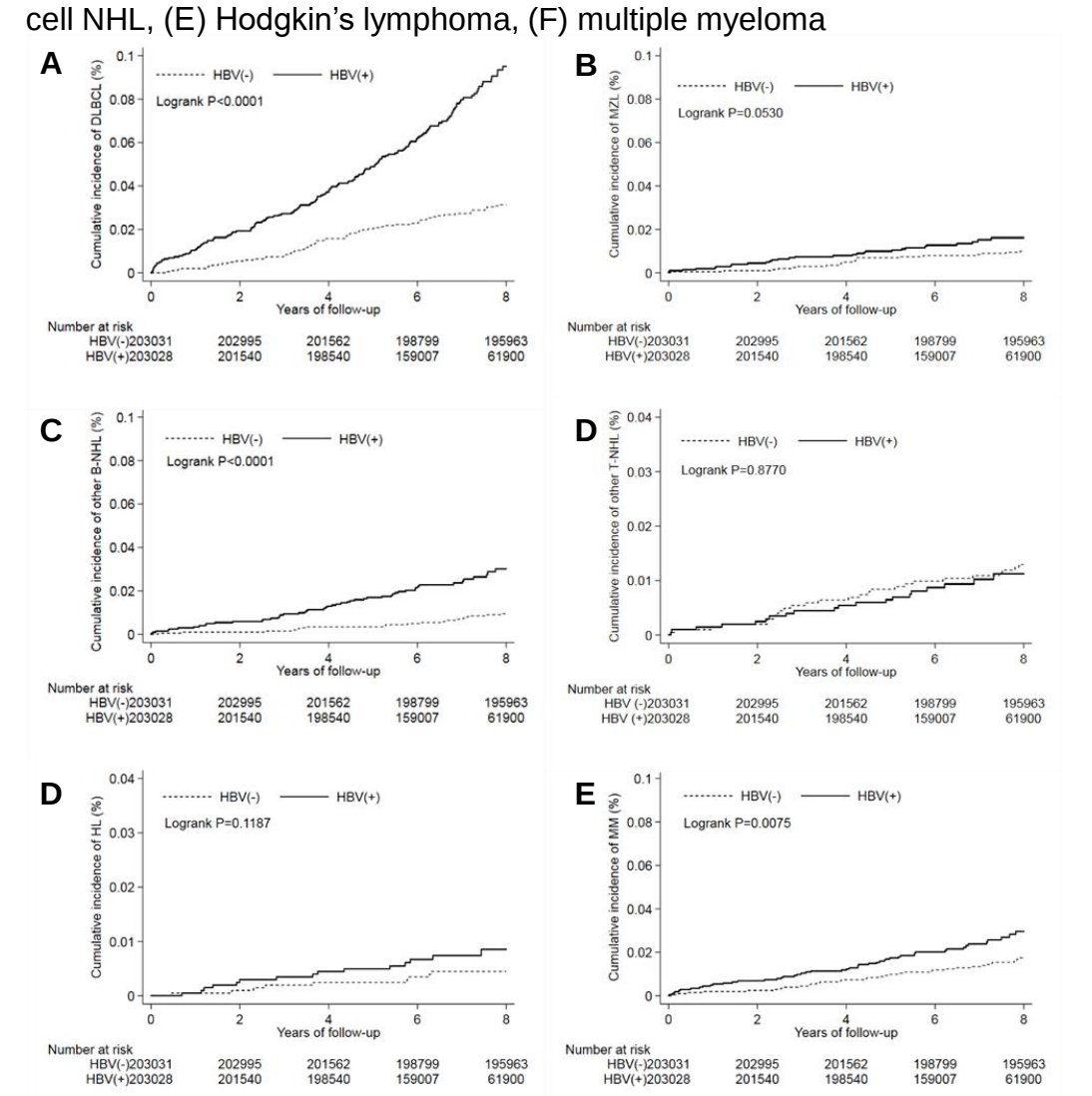


Table 1. Subtypes of lymphoma in the HBV and non-HBV cohorts

Subtypes	HBV cohort (n=421)	Non-HBV cohort (n=282)	HR[a]	95%CI	P
Non-Hodgkin's lymphoma, n(%)	309 (73.40)	193 (68.44)	2.35	1.94-2.84	<0.0001
Diffuse large B cell lymphoma, n(%)	169 (40.14)	88 (31.21)	2.84	2.16-3.73	<0.0001
Marginal zone lymphoma, n(%)	32 (7.60)	29 (10.28)	1.64	0.96-2.81	0.073
Lymphoplasmacytic lymphoma, n(%)	3 (0.71)	0 (0)	-	-	-
Other B cell lymphoma, n(%)	57 (13.54)	25 (8.87)	3.33	2.03- 5.48	<0.0001
T cell non-Hodgkin's lymphoma, n(%)	23 (5.46)	34 (12.06)	0.88	0.50-1.55	0.665
Other unspecified lymphoma, n(%)	25 (3.80)	17 (6.03)	1.67	0.86-3.22	0.127
Hodgkin's lymphoma, n(%)	16 (3.80)	11 (3.90)	1.83	0.83-4.02	0.134
Multiple myeloma, n(%)	56 (13.30)	49 (17.38)	1.67	1.11-2.51	0.014
Others[a] n(%)	40 (9.50)	29 (10.28)	2.39	1.43-4.01	0.001

*Including acute lymphoblastic leukemia, chronic lymphocytic leukemia