

Table 2.4. Case-control studies of Epstein-Barr virus infection markers and non-Hodgkin lymphoma (NHL)

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjusted potential confounders	Comments
Lei <i>et al.</i> (2000) Hong Kong 1998–1999	7 newly diagnosed cases of EBV-associated NHL or post-transplant lymphoproliferative disease	35 healthy controls	EBV DNA (<i>BAM</i> HI-W) in plasma by real-time quantitative PCR	EBV DNA No Yes	0 6	1.0 ∞	No	Characteristics of controls were unavailable. No control had detectable EBV DNA in plasma.
Hardell <i>et al.</i> (2001b) Sweden 1994–1997	33 newly diagnosed cases of histologically confirmed NHL	39 age-sex-matched patients operated for benign lesions	Anti-EBV VCA IgA and IgM and EA IgG by indirect immunofluorescence, and EBNA-1 IgG and IgM by ELISA (for 23 cases and 32 controls)	Anti-EBV EA IgG titre/TEQ $\leq 80/\leq 27.39$ $\leq 80/> 27.39$ $> 80/\leq 27.39$ $> 80/> 27.39$	5 4 4 8	1.0 0.75 (0.12–4.7) 0.94 (0.17–5.1) 2.8 (0.52–18)	Age, sex, body mass index	Median anti-EBV EA IgG titer in controls = 80; Median TEQ in controls = 27.39. The current exposure to dioxins & dibenzofurans in combination with EBV might increase the risk of NHL.
Hardell <i>et al.</i> (2001a) Sweden 1994–1997	67 newly diagnosed cases of histologically confirmed NHL	78 age-sex-matched controls selected from patients operated for benign lesions or the population register	Anti-EBV VCA IgG and IgM and EA IgG by indirect immunofluorescence, and EBNA-1 IgG and IgM by ELISA	Anti-EBV EA IgG titre >80 No Yes	27 39	1.0 1.9 (0.9–3.8)	Age, sex, body mass index	Median anti-EBV EA IgG titer in controls = 80. The OR associated with anti-EA IgG titre >80 was higher in those with elevated levels of PCBs, HCB, chlordanes and TBDE.

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Mitarnun <i>et al.</i> (2002) Thailand 1997–2000	100 newly diagnosed cases of histologically confirmed peripheral T-cell and NK-cell proliferative disease/lymphoma	100 age-sex-matched healthy volunteers living in study area. They had no history of serious illness, haematological diseases or fever within 1 month prior to enrollment.	Anti-EBV VCA, EA and EBNA by indirect immunofluorescence	Anti-VCA IgG <1:40 ≥1:40 Anti-EA IgG <1:10 ≥1:10 Anti-EBNA <1:20 ≥1:20	8 92 72 28 23 77	1.0 [5.4 (2.4–12.3)] 1.0 [3.5(1.6–7.5)] 1.0 0.7 [0.3–1.4]	No	Characteristics of controls were unavailable.
Berrington de González <i>et al.</i> (2006)	80 cases of NHL; Most cancers microscopically verified	588 patients admitted with a number of other cancer types (88 oral cavity, 53 cervix, 66 prostate, 83 HL, 203 leukaemia, 95 other cancers) and cardiovascular disease (n=101)	EBV EBNA ELISA (IgG recombinant EBNA-1 antigens)	Tertiles of optical density 0–3.81 3.82–5.29 5.30+ p for trend	24 31 22	1.00 1.32 (0.7–2.4) 0.87 (0.4–1.8) 0.80	Age, HIV, plate & day of assay	Bonferroni adjustment for multiple comparison

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De Sanjose <i>et al.</i> (2007) Europe	1085 newly diagnosed cases of histologically confirmed NHL	1153 age, sex and country matched controls	Abnormal reactive EBV antibody pattern. (ELISA combining immunodominant epitopes of EBNA-1 and VCA-p18; immunoblot analysis of distinct antibody diversity patterns to EBV EA, EBNA-1, VCA p-18, VCA-p40 and Zebra	Abnormal reactive patterns No Yes	826 259	1.0 1.42(1.15–1.74)	Age, sex, country, education	
Suwiwat <i>et al.</i> (2007) Thailand	45 newly diagnosed cases of histologically confirmed peripheral T-cell and NK-cell proliferative disease (7) /lymphoma (38)	45 age-sex-matched healthy volunteers living in the study area	EBV DNA (<i>Bam</i> HI-W) by real-time quantitative PCR	EBV DNA No Yes	8 37	1.0 0 (0–0.41)	No	Characteristics of controls were unavailable. No control had detectable EBV DNA.

TEQ, Dioxin-like toxic equivalent; HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; MM, multiple myeloma; ELISA, enzyme linked immunosorbent assay; PCR, polymerase chain reaction