Chronic hepatitis B virus infection is associated with a poorer prognosis in diffuse large B-cell lymphoma: a meta-analysis and systemic review

Running title: HBV and poorer prognosis in DLBCL

Xingyu Rong¹,²#, Hai Wang¹,²#, Jiexian Ma²#, Shaokun Pan¹, Huijing Wang²,³*, Sha Jing¹,⁴, Yu Su¹, Lancui Wang¹, Chao Zhao¹,²,⁴*

Supplementary Material

Legends for figure

Figure S1. Funnel plots for each comparison in the meta-analysis.
Figure S1

A. Two-year OS
B. Five-year OS
C. Two-year PFS
D. Five-year PFS
E. CR
F. PD
G. Over 60-years-old
H. Stage 3 or 4
I. Elevated LDH
J. B symptoms
K. IPI score
L. Extral-nodal metastasis
M. Subtype
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country (Hep B prevalence)</th>
<th>Study Design</th>
<th>Number of cases</th>
<th>Number of controls</th>
<th>Treatment of the DLBCL</th>
<th>Treatment for HBV infection</th>
<th>Hep B assessment (Yes/No)</th>
<th>DLBCL assessment</th>
<th>Assessment indexes</th>
<th>Matching and adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deng</td>
<td>2015</td>
<td>China (High)</td>
<td>cohort</td>
<td>81</td>
<td>506</td>
<td>All patients received a standard CHOP or R-CHOP as the primary treatment. Rituximab was not used on patients with HBV DNA level greater than 1 * 10^5 IU/ml.</td>
<td>Prophylactic antiviral therapy was used on HBsAg positive patients and HBsAg negative, anti-HBc positive patients up to 6 months after oncology treatment ends, HBV-DNA level.</td>
<td>Yes (HBeAg, HBeAb and HBV DNA were also detected)</td>
<td>Pathology confirmed all cases</td>
<td>age, stage of disease, bulky disease, B symptoms, number and site of extra nodal disease, IPI score and LDH level, hepatic dysfunction before and during chemotherapy, response to primary chemotherapy, OS, PFS</td>
<td>Patients were excluded from the study if they were HIV positive or anti-HCV positive.</td>
</tr>
<tr>
<td>Feng</td>
<td>2016</td>
<td>China (High)</td>
<td>case-control</td>
<td>36</td>
<td>124</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
<td>Yes (HBeAg, HBeAb were also detected)</td>
<td>Pathology confirmed all cases</td>
<td>age, stage of disease, number and site of extra nodal disease, IPI score, LDH level, hepatic dysfunction before and during chemotherapy</td>
<td>No patients were HIV positive</td>
</tr>
<tr>
<td>Guo</td>
<td>2015</td>
<td>China (High)</td>
<td>cohort</td>
<td>52</td>
<td>83</td>
<td>All patients received first-line treatment regimen—R-CHOP/CHOP/CHOP-like and most of them received MabThera. Parts of them received radiotherapy.</td>
<td>All 21 patients with active HBV infection received antiviral therapy (lamivudine and entecavir) for at least 6 months after the end of chemotherapy.</td>
<td>Yes (HBeAg, HBeAb and HBV DNA were also detected)</td>
<td>Pathology confirmed all cases</td>
<td>age, stage of disease, IPI score and LDH level, Hans typing</td>
<td>No patients were HIV positive</td>
</tr>
<tr>
<td>Author Year</td>
<td>Country</td>
<td>Case-Control</td>
<td>Case</td>
<td>Control</td>
<td></td>
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<td>Huang 2012</td>
<td>China (High)</td>
<td>case-control</td>
<td>38</td>
<td>270</td>
<td></td>
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<tr>
<td>Law 2015</td>
<td>Hong Kong (High)</td>
<td>case-control</td>
<td>16</td>
<td>65</td>
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<tr>
<td>Shan 2016</td>
<td>China (High)</td>
<td>case-control</td>
<td>76</td>
<td>159</td>
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</tbody>
</table>

All patients received first-line treatment regimen: R-CHOP/CHOP/CHOP-like.

Not mentioned

- Yes (HBeAg, HBeAb were also detected)
- Pathology confirmed all cases

- Age, stage of disease, number and site of extra nodal disease, IPI score, LDH level, hepatic dysfunction before and during chemotherapy, OS, PFS

- No patients were HIV positive

Stage I or II: four courses of CHOP(b) or R-CHOP(c)+regional radiation therapy(RT) to the involved area; Stage III or IV or early stage with bulky diseases: 8 courses of CHOP or R-CHOP. RT was given to patients with bulky tumors.

HBsAg positive patients received lamivudine prophylaxis, (from the beginning of chemotherapy to 6 months after completion of chemotherapy)

- Yes
- Pathology confirmed all cases

- Age, stage of disease, bone marrow involvement with lymphoma, bulky disease, B symptoms, number and site of extra nodal disease, IPI score and LDH level, hepatic dysfunction before and during chemotherapy, OS

Patients were excluded from the study if they were HIV positive or anti-HCV positive.

All patients received more than 4 circles CHOP or R-CHOP treatment

Not mentioned

- Yes (HBeAg, HBeAb were also detected)
- Pathology confirmed all cases

- Age, stage of disease, bone marrow involvement with lymphoma, bulky disease, B symptoms, number and site of extra nodal disease, IPI score and LDH level, hepatic dysfunction before and during chemotherapy, Han typing, OS, PFS

No patients were HIV positive
<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Case-Control</th>
<th>Cases</th>
<th>Controls</th>
<th>Follow-up</th>
<th>Study Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wang 2016</td>
<td>China (High)</td>
<td>case-control</td>
<td>52</td>
<td>200</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
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<tr>
<td>Wang 2018</td>
<td>China (High)</td>
<td>case-control</td>
<td>120</td>
<td>388</td>
<td>Standard chemotherapy based on the first-line regimen of CHOP or R-CHOP</td>
<td>Not mentioned</td>
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<tr>
<td>Wei 2015</td>
<td>China (High)</td>
<td>case-control</td>
<td>33</td>
<td>117</td>
<td>Not mentioned</td>
<td>Not mentioned</td>
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<tr>
<td>Wei 2014</td>
<td>China (High)</td>
<td>case-control</td>
<td>59</td>
<td>235</td>
<td>All patients received 6-8 cycles of first-line CHOP or R-CHOP-like regimens.</td>
<td>Not mentioned</td>
</tr>
</tbody>
</table>
Zheng 2014 China (High) cohort 56 328

All patients received at least four cycles of first-line CHOP-or R-CHOP-like regimens and had at least a follow-up of 3 months. No treatment on HBV infection. Yes Pathology confirmed all cases age, stage of disease, number and site of extra nodal disease, Hans typing

Patients with HCV or HIV infection and primary central nervous system lymphoma cases were excluded in this study.