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# 652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

## Hepatitis B Virus Infection Status and Reactivation Analysis in Multiple Myeloma in China

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#### Background:

China is a highly endemic area for Hepatitis B virus (HBV) infection and HBV reactivation is an event of concern in treating patients with hematologic malignancy. However, there were very few reports regarding HBV reactivation in patients with multiple myeloma (MM) in China. Since the approval of novel agents, especially immunotherapy such as monoclonal antibody and chimeric antigen T cell immunotherapy, the risk of HBV reactivation has increased. Therefore, the study aimed to evaluate the HBV infection status in MM and explore the incidence and risk factors of HBV reactivation in MM patients in China. Methods:

Newly diagnosed MM patients with available serologic assays for HBV infection were retrospectively enrolled between June 30, 2008 and December 30, 2022 in West China Hospital, Sichuan University. Demographic and clinical data were obtained from the "HemaTank" Chinese Multiple Myeloma Database (HCMMD). Meanwhile, patients diagnosed with Waldenstrom Macroglobulinemia (WM) at the same time were enrolled as the control group. HBV reactivation was defined as the occurrence of one of the following:  $\geq$  2 log increase in HBV-DNA levels from baseline level, detection of HBV-DNA with level > 100 IU/ml in a person with undetectable HBV DNA at baseline or HBsAg-negative becoming positive. The penalized maximum likelihood logistic regression for rare events was applied to identify independent risk factors related to HBV reactivation. Results:

The study recruited 3040 MM patients with a median age of 62 (range 14798) and 240 WM patients with a median age of 63 (range 25'92). The HBsAg-positive rates were similar between MM and WM (9.4% vs 10.8%, P=0.49), but both the HBcAbpositive rates and HBeAb-positive rates in WM were significantly higher than MM (76.3% vs 60.7%, P<0.001; 37.5% vs 25.1%, P<0.001). The analysis of co-expression of HBV markers shows that the prevalence of HBsAg-/Anti-HBs+/anti-HBC- in MM was significantly higher than WM (16.7% vs 8.3%, P<0.001) and HBsAg-/Anti-HBs-/anti-HBC+ in MM was significantly lower than WM (18.3% vs 27.1%, P<0.001). However, he prevalence of HBsAg+/ HBeAg+/anti-HBC+ and HBsAg+/ anti-HBeAb+/anti-HBC+ were similar between MM and WM (0.5% vs 1.3%, P=0.158; 8.6% vs 8.8%, P=0.503). The baseline characteristics of HBsAq-positive MM and HBsAq-negative MM were summarized in Table 1. The rates of HBsAq-positive MM were significantly increased in young male patients (P<0.05). The level of ALT and AST, and the incidence of HBV reactivation, liver cirrhosis and pulmonary disease were significantly higher in HBsAg-positive MM than in HBsAg-negative MM (P<0.05). Of the 2147 MM patients who have received at least one line of chemotherapy (Table 1), 924 (43%) MM patients received bortezomib-containing or lenalidomide-containing regimens as the frontline therapy, while only 21 (1.0%) received a daratumumab-containing regimen as the frontline therapy. During hospital-documented follow-up visits, 26 (1.21%) MM patients have experienced HBV reactivation. According to the multivariate analysis of risk factors for HBV reactivation in MM, liver cirrhosis (OR 8.63, 95%CI 2.95-25.24, P<0.001), autologous stem cell transplantation (OR 6.03, 95%Cl 2.47-14.72, P<0.001) and HBsAg-positive (OR 14.45, 95%CI 6.50-32.14, P<0.001) were independent risk factors associated with high prevalence of HBV reactivation. The ROC curve of the model integrating the three factors is shown in Figure 1, and the AUC was 0.8584. Conclusions:

Among Chinese MM patients with multiple myeloma, a high proportion of MM patients presented with resolved hepatitis B virus infection, whereas HBV reactivation was pretty rare. However, long-term HBV DNA levels monitoring is still needed for MM patients at high risk for HBV reactivation.

Table 1. The baseline characteristics of HBsAg-positive MM and HBsAg-negative MM.

## **Disclosures** No relevant conflicts of interest to declare.

	HBsAg-postive MM a=287	HBiAg-negative MM n=2753	P-value		HBsAg-positive MM n=287	HBsAg-negative MM n=2753	P-value
Age, mean ± SD	58.87 ± 11.14	61.44 ± 12.04	<0.001	HBV reactivation			
Gender				No	271 (94.4%)	2743 (99.6%)	<0.001
Female	103 (35.9%)	1238 (45.0%)	0.003	Yes	16 (5.6%)	10 (0.4%)	
Male	184 (64, 1%)	1515 (55.0%)		Fatty liver disease			
BML mean ± SD	22.79 ± 2.90	23.03 ± 3.18	0.50	No	259 (90.2%)	2447 (88.9%)	0,48
Smoking history				Yes	28 (9.8%)	306 (11.1%)	
No	55 (82,1%)	659 (82,2%)	0.99	Liver cirrhosis			
Yes	12 (17.9%)	143 (17.8%)		No	268 (93.4%)	2674 (97.1%)	-0.001
Alcohol consumption				Yes	19 (6.6%)	79 (2.9%)	
No	54 (80.6%)	698 (86.9%)	0.15	Tuberculosis			
Yes	13 (19.4%)	105 (13.1%)		No	283 (98.6%)	2676 (97.2%)	0.16
Hb (g/L), mean ± SD	$102.84 \pm 31.99$	$98.44 \pm 29.44$	0.020	Yes	4(1.4%)	77 (2.8%)	
PLT (×10°9/L), mean ± SD	$152.44 \pm 83.63$	171.66 ± 95.20	0.001	Hypertension			
WBC (~10*9/L), mean ± SD	6.16 ± 2.65	$6.58 \pm 4.87$	0.15	No	219 (76.3%)	2045 (74.3%)	0.45
Lymphocyte (×10°9/L), mean ± SD	$1.58 \pm 0.79$	$1.61 \pm 1.16$	0.65	Yes	68 (23.7%)	708 (25.7%)	
Neutrophils, mean ± SD	$3.94 \pm 2.25$	$4.32 \pm 3.87$	0.11	Diabetes mellitus			
CD3+ T cell (%), mean ± SD	$69.38 \pm 13.80$	$69.62 \pm 12.29$	0.88	No	258 (89.9%)	2449 (89.0%)	0.63
CD4+ T cell (%), mean ± SD	$35.45 \pm 11.38$	$35.41 \pm 11.17$	0.98	Yes	29(10.1%)	304 (11.0%)	
CD8+ T cell (%), mean ± SD	$29.42 \pm 11.27$	$30.12 \pm 11.72$	0.64	Renal insufficiency			
Ca, mean ± SD	$2.28 \pm 0.38$	$2.27 \pm 0.38$	0.66	No	235 (81.9%)	2214 (80.4%)	0.55
LDH (U/L), median (JQR)	192.00 (152.00, 251.00)	184.50 (147.00, 244.00)	0.23	Yes	52 (18.1%)	539 (19.6%)	
Cr. median (IQR)	85.00 (65.30, 167.00)	84.95 (65.30, 139.00)	0.55	Amylesis			
ALT, median (IQR)	21.00 (14.50, 31.50)	17.00 (12.00, 27.00)	<0.001	No	271 (94.4%)	2522 (91.6%)	0.097
AST, median (IQR)	24.50 (18.00, 33.00)	22.00 (17.00, 30.00)	0.001	Yes	16 (5.6%)	231 (8.4%)	
Albumin, mean ± SD	$36.57 \pm 7.83$	36.06 ± 7.98	0.31	Pulmonary disease			
Beta-2 microglobulin, median (JQR)	4.78 (2.67, 11.10)	4.33 (2.77, 8.37)	0.40	No	215 (74.9%)	1862 (67.6%)	0.012
IgG, median (IQR)	12.30 (5.50, 33.35)	12.00 (5.96, 33.05)	0.65	Yes	72 (25.1%)	891 (32.4%)	
gA, median (IQR)	900.00 (247.00, 2915.00)	715.00 (229.00, 3180.00)	0.34	autologous stem cell transplantation			
IgM, median (IQR)	371.00 (168.50, 838.00)	336.00 (161.00, 728.00)	0.11	No	260 (90.6%)	2561 (93.0%)	0.13
mmunoparesis				Yes	27 (9.4%)	192 (7.0%)	
No	56 (22.2%)	448 (18.3%)	0.12	Frontline treatment	N=209	N=1938	0.056
Yes	196 (77.8%)	2006 (81.7%)		Daratamumab-containing regimen	0(0)	21 (1.1)	
ISS stage				Boetezomib/lenalidomide-			
1	61 (29.8%)	577 (30.4%)	0.068	containing regimen	7 (3.3)	143 (7.4)	
ш	48 (23.4%)	571 (30.1%)		Bortezomib-containing regimen	58 (27.8)	584 (30.1)	
ш	96 (46.8%)	747 (39.4%)		lenalidomide-containing regimen	16 (7.7)	116 (6.0)	
				Thalidomide-containing regimen	95 (45.5)	850 (43.9)	
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Pactors	Odds ratio	Standard error		lower limit	upper limit	
Liver cirrhosis	8.63	4.73	<0.001	2.95	25.24	
ASCT	6.03	2.75	< 0.001	2.47	14.72	
HBsAg-positive	14.45	5.89	< 0.001	6.50	32.14	

Figure 1. The ROC curves of the penalized maximum likelihood logistic regression model combining factors of liver cirrhosis, autologous stem cell transplantation and HBsA<sub>2</sub> possitive status used to predict the risk of HBV reactivation in MM receiving chemotherapy.

Figure 1

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