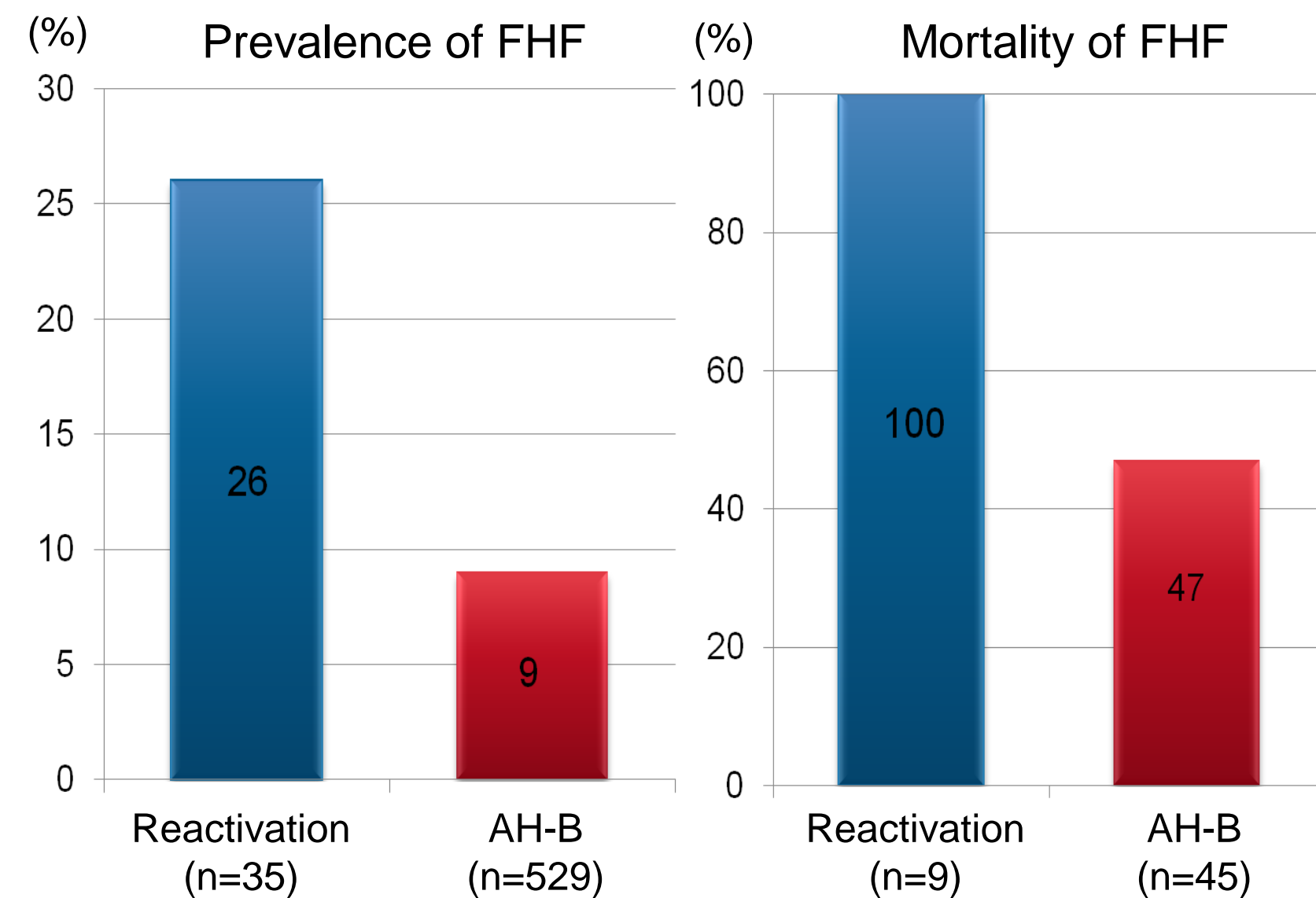


Clinical and Virological Features of Patients with Fulminant Hepatic Failure Due to Hepatitis B Virus Reactivation from HBsAg-negative Status

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Background

Reactivation of hepatitis B virus (HBV) in subjects with resolved HBV infection (HBsAg-negative, anti-HBc-positive, and/or anti-HBs-positive) has been reported in increasing numbers in patients undergoing cytotoxic chemotherapy or immunosuppressive therapy. We previously reported that HBV reactivation in subjects with resolved HBV infection having undergone chemotherapy is as high as 4% of newly developed HBsAg-positive HBV cases in Japan. (Umemura T *et al.* Clin Infect Dis 2008) One-fourth of HBV reactivation cases develop into fulminant hepatic failure (FHF), and mortality among these patients is 100%.



Aim

Since the exact virological characteristics of HBV reactivation have not been fully clarified in this setting, the present study investigated the clinical significance and virological features of HBV reactivation leading to FHF.

Patients and Methods

We recruited a total of 564 patients between January 2000 and December 2008 who had become newly-positive for serum HBsAg. Thirty-five individuals were found to have HBV reactivation after resolved HBV infection, and the remaining 529 patients were classified as having acute hepatitis B.

Conclusions

Although genotype A was not found in patients with HBV reactivation, genotype B was relatively frequent in such Japanese patients. HBV genotype, HBV DNA levels, G1896A mutation, or A1762T/G1764A mutations did not influence the development of FHF in HBV reactivation cases, but the G1896A mutation tended to progress more often to FHF in patients with genotype B.

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	Reactivation (N=23)	AH-B (N=529)	P
Age	63	33	<0.001
Male	59%	71%	>0.2
Liver function			
ALT (IU/L)	929	2300	<0.001
T Bil (mg/dL)	10.3	6.4	0.12
Alb (g/dL)	3.2	3.6	<0.001
PT (%)	65.0	75.0	>0.2
HBV DNA (log copies/ml)	7.5	5.5	<0.001
HBV genotype	(N=19)	(N=232)	
A	0%	25%	0.003
B	42%	12%	<0.001
C	58%	63%	>0.2

	FHF (N=9)	non-FHF (N=26)	P
Age	65	62	>0.2
Male	44%	62%	>0.2
NHL	100%	54%	0.012
Rituximab regimen	90%	39%	0.011
Lamivudine use	100%	92%	>0.2
Liver-related death	100%	4%	<0.001

	FHF (N=9)	non-FHF (N=26)	P
Liver function			
ALT (IU/L)	924	1230	>0.2
T Bil (mg/dL)	28.4	5.9	0.001
Alb (g/dL)	2.8	3.3	0.004
PT (%)	20.6	72.5	<0.001
HBV DNA (log copies/ml)	6.9	7.5	>0.2
HBV genotype			
Bj	3/8 (38%)	7/19 (37%)	>0.2
C	5/8 (63%)	12/19 (63%)	
PC mutation	6/8 (75%)	6/16 (38%)	0.10
CP mutation	3/8 (38%)	5/16 (31%)	>0.2