

INTRODUCTION

- As the number of reports of hepatitis B virus (HBV) reactivation increases in patients with HBV/HCV co-infection with direct-acting antiviral (DAA) agents, the US Food and Drug Administration has issued warnings about the potential risk of HBV reactivation in these patients.
- So far, there are very limited clinical data.

AM

- To report the efficacy of anti-HCV treatment in CHC patients co-infected with HBV
- To report the HBV reactivation rate in CHC patients co-infected with HBV during and afer anti-HCV treatment
- To elucidate the factors affecting HBV reactivation in CHC patients co-infected with HBV during and after anti-HCV treatment

3 METHOD

- Retrospective observational study
- 62 patients with HBV/HCV co-infection between January 2005 and April 2018 at the Pusan National University Hospital
- Definition of HBV reactivation
 - $\geq 1 \log_{10}$ increase in HBV replication from baseline levels

or

 new appearance of HBV DNA in patient with previously undetectable levels

Table 1.

	Sex	Age	HCV	HCV treatment	SVR	Initial	Initial	HBV reactivation							NUC	F/U
			GT			HCV RNA (IU/mL)	HBV DNA (IU/mL)	Time	HBV ALT DNA (IU/mL)		Peak HBV DNA (IU/mL)	Peak ALT	Recovery	HBV DNA (IU/mL)	⁻ therapy	(days)
1	Μ	39	3	IFN	Yes	1320000	129	149 wks after Tx. termination	1510	13	2360	35	561 wks after Tx. termination	<20	No	4188
2	F	56	1b	IFN	Yes	3140000	Not detected	113 wks after Tx. discontinuation	28	26	778	26	279 wks after Tx. discontinuation	335	No	2135
3	F	80	1b	D+A, 24wks	Yes	62000	42	4 wks after Tx. initiation	7480	17	7480	35	12 wks after Tx. initiation	<20	No	295
4	F	69	2	S+R, 16wks	Yes	1890000	Not detected	38 wks after Tx. termination	35	14	35	14	51 wks after Tx. termination	<20	No	456
5	F	76	1b	OBV/PTV/r+DSV, 12wks	Yes	502000	Not detected	12 wks after Tx. initiation	835	23	835	23	12 wks after Tx. termination	<20	No	85
6	F	63	1b	D+A, 24wks	Yes	1390000	Not detected	12 wks after Tx. initiation	42	26	42	113	16 wks after Tx. initiation	<20	No	270
7	F	66	1b	IFN \rightarrow D+A, 10wks	No	6700000	Not detected	52 wks after Tx. discontinuation	114	76	114	76	Transfer		No	367
8	Μ	48	1b	IFN \rightarrow D+A, 24wks	Yes	1300000	Not detected	48 wks after Tx. termination	9180	47	9180	47	Ongoing follow up		No	337
9	F	74	1b	IFN \rightarrow D+S, 12wks	Yes	3410000	102	4 wks after Tx. initiation	22900	11	22900	11	12 wks after Tx. initiation	<20	No	437
10	Μ	52	1b	IFN \rightarrow OBV/PTV/r+DSV, 12wks	Yes	452000	Not detected	4 wks after Tx. initiation	46	14	197	16	12 wks after Tx. initiation	Not detected	No	169
11	F	55	1b	IFN \rightarrow D+A, 24wks	Yes	3580000	<20	16 wks after Tx. initiation	693	24	1010	42	24 wks after Tx. termination	<20	No	253

The risk of HBV reactivation among HBV/HCV co-infected patients treated with direct-acting antiviral agents : A single center experience

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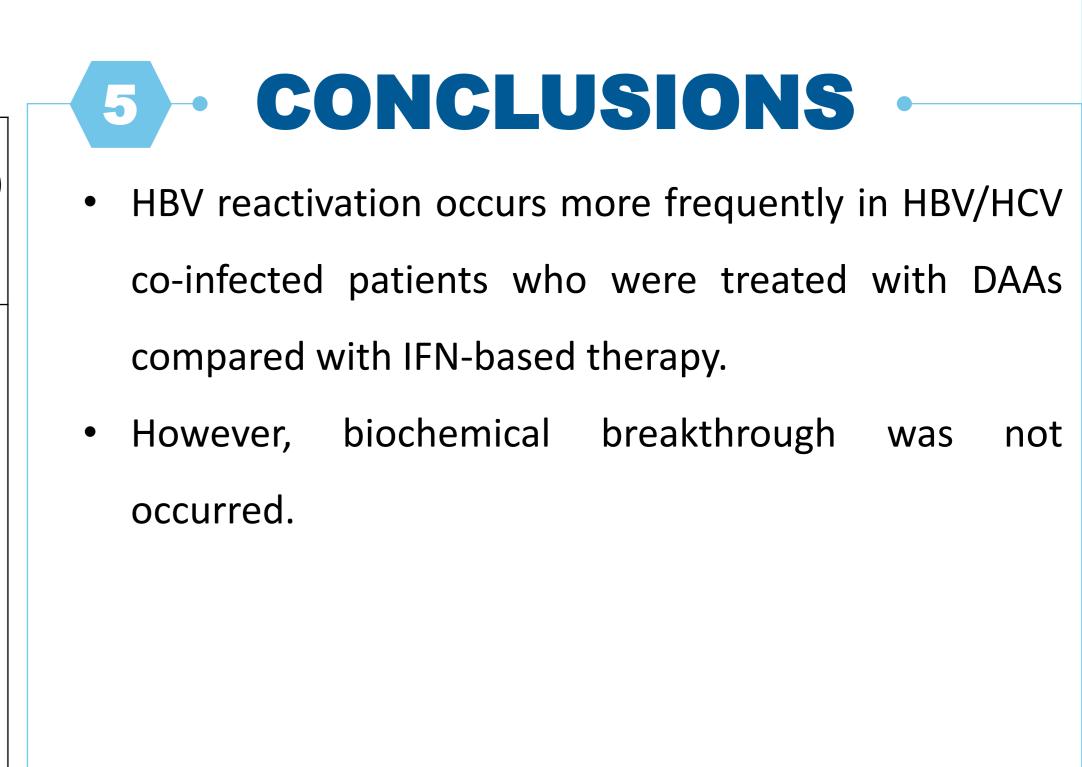
RESULTS

		Treatment grou	n				Treatment g	roup			
		in eatment grou	DAA					DAA			
	IFN only	DAA after				IFN only	DAA afte		A only		
	(n = 25)		f IFN			(n = 25)	treatment failu	re of IFN	-		
		(n = 9)	(n = 15)				(n = 9)	1)	ו = 15)		
		1	9/24 (79.2)					9/24 (37.5)			
SVR, n (%) 20	0/34 (61.8)	7/9 (77.8)	12/15 (80.0)	HBV reactivation, n (%)	2 (8.0)	5/9 (55.6)		4/15 (26.7)		
Table 4. Predictive factors	affecting	HBV reactivation									
Characteristics		No HBV reactivation N = 38	HBV reactivation N = 11	P value	Characteristics		No HBV reactivation N = 38	HBV reactivatio N = 11	n <i>P</i> value		
Sex, n (%)				0.037	Treatment group, n (%)				0.010		
Male		25 (65.8)	3 (27.3)		IFN only		23 (60.5)	2 (18.2)			
Female		13 (34.2)	8 (72.7)		DAA only		11 (28.9)	4 (36.4)			
Age, mean ± SD		64.2 ± 8.5	61.6 ±12.8	0.147	DAA after treatment failure of IFN		4 (10.5)	5 (45.5)			
HCV genotype, n (%)				0.039	Experience of DAA treatment, n (%)				0.013		
1b		18 (47.4)	9 (81.8)		No		23 (60.5)	2 (18.2)			
2		18 (47.4)	1 (9.1)		Yes		15 (39.5)	9 (81.8)			
3		0 (0.0)	1 (9.1)		Presence of cirrhosis, n (%)				0.492		
5		1 (2.6)	0 (0.0)		No		22 (57.9)	8 (72.7)			
4							16 (12 1)	3 (27.3)			
		1 (2.6)	0 (0.0)		Yes		16 (42.1)	5 (27.5)			
4	± SD	1 (2.6) 56.4 ± 48.8	0 (0.0) 49.5± 47.8	0.679	Yes		10 (42.1)	5 (27.5)			

Value 63 ± 11 5 (59.7) / (40.3)			Treatment group					Treatment g	roup		
								•			
		IFN only (n = 25)	DAA after treatment failure of (n = 9)	ent failure of IFN (n = 15)			IFN only (n = 25)	DAA afte treatment failur (n = 9)	re of IFN	A only = 15)	
33 (53.2)		20/34 (61.8)						9/24 (37.5)			
21 (33.9)	SVR, n (%)		7/9 (77.8)	12/15 (80.0)		HBV reactivation, n (%)	2 (8.0)	5/9 (55.6)		4/15 (26.7)	
1 (1.6) 3 (4.8) 3 (4.8)	Table 4. Predictive facto										
	Characteristics	5	No HBV reactivation N = 38			Characteristics	Nol	No HBV reactivation N = 38		P value	
	Sex. n (%)				0.037	Treatment group, n (%)		23 (60.5)		0.010	
23 (37.1)	Male		25 (65.8)	3 (27.3)		IFN only			2 (18.2)		
13 (21.0)	Female		13 (34.2)	8 (72.7)		DAA only		11 (28.9)	4 (36.4)		
25 (33.9)	Age, mean ± SD HCV genotype, n (%)		64.2 ± 8.5	61.6 ±12.8				4 (10.5)	5 (45.5)	0.013	
15 (24.2)			18 (47.4)	9 (81.8)				23 (60.5)	2 (18.2)		
9 (14.5)	2		18 (47.4)			Yes					
	3		0 (0.0)	1 (9.1)		Presence of cirrhosis. n (%)				0.492	
10 (41.7)	4		1 (2.6)	0 (0.0)				22 (57.9)	8 (72.7)		
8 (33.3)	Not detected		1 (2.6)	0 (0.0)				16 (42.1)	3 (27.3)		
1 (4.2)	ALT level before treatment, m	iean ± SD	56.4 ± 48.8	49.5± 47.8	0.679						
5 (20.8)	HCV RNA level before treatme	ent, mean ± SD	$3.31^*10^6 \pm 5.54^*10^6$	$2.16*10^6 \pm 1.93*10^6$	⁶ 0.294						
0.3 ± 44.3 $10^6 \pm 4.64^*10^6$	✓ On multivariate anal	yses, the exp	perience of DAA (od	ds ratio [OR] 19	.306, 95%	6 confidence interval [CI] 1.600)—107.825,	<i>P</i> = 0.016) and	female (OR 13.	193, 95%	
21 1 3 23 13 25 15 9 10 8 1 5 0.3	1 (33.9) 1 (1.6) 1 (1.6) 3 (4.8) 3 (4.8) 3 (37.1) 3 (21.0) 5 (33.9) 5 (24.2) 0 (14.5) 0 (41.7) 3 (33.3) 1 (4.2) 5 (20.8)	1 (33.9) SVR, n (%) 1 (1.6) Table 4. Predictive factor 1 (1.6) Table 4. Predictive factor 3 (4.8) Characteristics 3 (4.8) Sex, n (%) 3 (4.8) Sex, n (%) 3 (37.1) Male Female Age, mean \pm SD 4 Solution 5 (33.9) HCV genotype, n (%) 5 (24.2) 1b 9 (14.5) 2 3 Not detected 1 (4.2) ALT level before treatment, m 6 (20.8) HCV RNA level before treatment, m 3 \pm 44.3 \checkmark On multivariate anal	1 (33.9) SVR, n (%) $20/34$ (61.8) 1 (1.6) Table 4. Predictive factors affecting 3 (4.8) Characteristics 3 (4.8) Sex, n (%) 3 (37.1) Male Female Female 3 (21.0) Age, mean \pm SD 5 (33.9) HCV genotype, n (%) 5 (24.2) 1b 9 (14.5) 2 3 0 (41.7) 4 (33.3) 0 (41.7) 4 4 (33.3) Not detected 1 (4.2) ALT level before treatment, mean \pm SD 4 (20.8) HCV RNA level before treatment, mean \pm SD 3 \pm 44.3 (O and bit is is the method is the	SVR, n (%) $20/34$ (61.8) $7/9$ (77.8) 1 (1.6) Table 4. Predictive factors affecting HBV reactivation 3 (4.8) Characteristics No HBV reactivation 3 (4.8) Characteristics No HBV reactivation 3 (4.8) Sex, n (%) N = 38 3 (37.1) Male 25 (65.8) Female 13 (34.2) Age, mean \pm SD 64.2 \pm 8.5 HCV genotype, n (%) 5 (24.2) 1b 18 (47.4) 3 0 (0.0) 0 (41.7) 4 1 (2.6) 1 (4.2) Alt level before treatment, mean \pm SD 56.4 \pm 48.8 0 (20.8) HCV RNA level before treatment, mean \pm SD 3.31*10 ⁶ \pm 5.54*10 ⁶ 3 \pm 44.3 $$ On multivariate analyses, the experience of DAA (od	SVR, n (%) 20/34 (61.8) 7/9 (77.8) 12/15 (80.7) 1 (1.6) Table 4. Predictive factors affecting HBV reactivation HBV reactivation 3 (4.8) Characteristics No HBV reactivation HBV reactivation 3 (4.8) Sex, n (%) $N = 38$ N = 11 3 (4.8) Sex, n (%) Male 25 (65.8) 3 (27.3) 3 (37.1) Male 25 (65.8) 3 (27.3) Female 13 (34.2) 8 (72.7) Age, mean ± SD 64.2 ± 8.5 61.6 ± 12.8 F(V genotype, n (%) 18 (47.4) 9 (81.8) 1 (14.5) 2 18 (47.4) 9 (81.8) 2 (41.7) 4 1 (2.6) 0 (0.0) 1 (2.6) 0 (0.0) 1 (9.1) 3 (20.8) Not detected 1 (2.6) 0 (0.0) 1 (4.2) ALT level before treatment, mean ± SD 56.4 ± 48.8 49.5 ± 47.8 (20.8) HCV RNA level before treatment, mean ± SD 3.31*10 ⁶ ± 5.54*10 ⁶ 2.16*10 ⁶ ± 1.93*10 3 ± 44.3 y^6 On multivariate analyses, the experience of DAA (odds ratio [OR] 19 19	SVR, n (%) 20/34 (61.8) 7/9 (77.8) 12/15 (80.0) 1 (1.6) Table 4. Predictive factors affecting HBV reactivation HBV reactivation P value 3 (4.8) Characteristics No HBV reactivation P value 3 (4.8) Sex, n (%) 0.037 3 (4.8) Male 25 (65.8) 3 (27.3) Female 13 (34.2) 8 (72.7) Age, mean ± SD 64.2 ± 8.5 61.6 ± 12.8 0.147 5 (24.2) 1b 18 (47.4) 9 (81.8) 0.039 5 (24.2) 1b 18 (47.4) 1 (9.1) 0.039 5 (24.2) 1b 18 (47.4) 1 (9.1) 0.039 5 (24.2) 1b 18 (47.4) 9 (81.8) 0.039 6 (4.2 ± 8.5 61.6 ± 12.8 0.147 0.039 0.000 1 (9.1) 3 (27.3) X 0 (0.0) 1 (9.1) 0.000 1 (9.1) 0.039 6 (24.2) 1b 18 (47.4) 9 (81.8) 0.000 1 (9.1) 0.000 1 (9.1) 0.000 1 (9.1) 0.000 1 (9.1) 0.000 1 (9.1) 0.000	Image: Sum (%) 20/34 (61.8) $7/9 (77.8)$ $12/15 (80.0)$ HBV reactivation, $n (\%)$ 1(1.6) Table 4. Predictive factors affecting HBV reactivation P value Characteristics 3(4.8) Characteristics No HBV reactivation P value Characteristics 3(4.8) Characteristics No HBV reactivation P value Characteristics 3(4.8) Sex, $n (\%)$ 0.037 Treatment group, $n (\%)$ IFN only 3(37.1) Sex, $n (\%)$ 0.037 Treatment group, $n (\%)$ IFN only 3(37.1) Sex, $n (\%)$ 0.037 Treatment group, $n (\%)$ DAA after treatment failure of IFN 3(37.1) Male 25 (65.8) 3 (27.3) IFN only DAA after treatment failure of IFN 3(32.0) Age, mean \pm SD 64.2 \pm 8.5 61.6 \pm 12.8 0.147 DAA after treatment failure of IFN 5 (33.9) HCV genotype, $n (\%)$ 18 (47.4) 9 (81.8) No No 9 (14.5) 2 18 (47.4) 1 (9.1) Yes Yes 10 (41.7) 4 1 (2.6) 0 (0.0) No Yes (20.8)	Mail SVR, n (%) 20/34 (61.8) 7/9 (77.8) 12/15 (80.0) 1 (1.6) Table 4. Predictive factors affecting HBV reactivation 12/15 (80.0) HBV reactivation, n (%) 2 (8.0) 3 (4.8) Characteristics No HBV reactivation P value Characteristics No 3 (37.1) Sex, n (%) Characteristics No HBV reactivation P value Characteristics No 3 (37.1) Male 25 (65.8) 3 (27.3) IFN only DAA only DAA only 3 (37.1) Male 25 (65.8) 3 (27.3) DAA only Experience of DAA treatment, n(%) 1 (14.5) 2 10 (0.0) 1 (9.1) Yes Yes	SVR, n (%) 20/34 (61.8) 7/9 (77.8) 12/15 (80.0) HBV reactivation, n (%) 2 (8.0) 5/9 (55.6) 11 (1.6) Table 4. Predictive factors affecting HBV reactivation No HBV reactivation P value Characteristics No HBV reactivation N = 38 N = 36 N = 36 <t< td=""><td>1 (3.3.9) SVR, n (%) 20/34 (61.8) 7/9 (77.8) 12/15 (80.0) HBV reactivation, n (%) 2 (3.0) 5/9 (55.6) 4/15 11 (1.6) Table 4. Predictive factors affecting HBV reactivation No HBV reactivation No No No HBV reactivation HBV reactivation No HBV reactivation No</td></t<>	1 (3.3.9) SVR, n (%) 20/34 (61.8) 7/9 (77.8) 12/15 (80.0) HBV reactivation, n (%) 2 (3.0) 5/9 (55.6) 4/15 11 (1.6) Table 4. Predictive factors affecting HBV reactivation No HBV reactivation No No No HBV reactivation HBV reactivation No HBV reactivation No	

Table 5. Virological characteristics of patients experience HBV reactivation during or after anti viral therapy for CHC

CI 1.614-107.825, P = 0.020) were significant factors associated with HBV reactivation after HCV treatment.





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