

# HBsAg+活体供肾移植给 HBsAg-受者： 来自中国的临床研究结果

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# BACKGROUND

- Utilization of HBsAg+ donors can expand the donor pool: 3.5%
- HBsAg+ kidneys seldom transplanted to HBsAg- recipients
- HBV immunity and HBV prophylaxis
- Underestimation/over-estimation of HBV transmission risk
- China: 93 million, 7.18%

- **KDIGO:** HBsAg+ donors may be considered for HBsAg- recipients with HBV immunity.
- **OPTN:** 0.0% in deceased and 0.5% in living.
- If **HBV DNA+**, most centers do not consider for D(HBsAg+)/R(HBsAg-) living donation.
- D(HBsAg+)/R(HBsAg-) KTx in **recipients without HBV immunity** have never been reported.
- These 2 types of KTx are actually performed in our center.



# METHODS

- Living D(HBsAg+)/R(HBsAg-) were retrospectively identified, West China Hospital from January 1, 2009 to June 30, 2017.
- Exclusion: (i) pre-transplant HCV infection, (ii) ABOi KTx, or (iii) deceased donor KTx
- D(HBcAb+)/R(HBcAb-) living KTx was used as the control group.
- Primary endpoint: post-transplant HBsAg-→+ in the recipient.



# RESULTS

**Table 1.** Baseline demographic, clinical and immunological characteristics in the two groups

	D(HBsAg+)/ R(HBsAg-) group (n=83)	D(HBcAb+)/ R(HBcAb-) group (n=384)	P value
<b>Donor</b>			
Median age, year (range)	50 (31-66)	48 (20-66)	0.302
Male (%)	39 (47.0)	132 (34.4)	<b>0.031</b>
Living related (%)	83 (100)	384 (100)	/
<b>Recipient</b>			
Median age, year (range)	32 (9-51)	28 (9-58)	<b>0.005</b>
Male (%)	64 (77.1)	269 (70.1)	0.197
<b>Cause of end stage renal failure</b>			
Glomerulonephritis (%)	40 (48.2)	65 (16.9)	<b>&lt;0.001</b>
Non-glomerulonephritis (%)	8 (9.6)	33 (8.6)	
Unknown (%)	35 (42.2)	286 (74.5)	
Preemptive transplant (%)	6 (7.2)	28 (7.3)	1.000
Median duration on dialysis, months (range)	9 (0-120)	10 (0-96)	0.182
Mean HLA mismatch (A, B, DR, DQ)	4.04±1.47	3.58±1.27	<b>0.004</b>
PRA>0(%)	27 (32.5)	96 (25%)	0.158
Second transplant	0	1 (0.3)	1.000
<b>Induction therapy</b>			
IL-2 receptor antagonist (%)	49 (59.0)	231 (60.2)	0.567
Antithymocyte globulin (%)	18 (21.7)	66 (17.2)	
No induction (%)	16 (19.3)	87 (22.7)	
<b>Initial immunosuppression</b>			
Tac+MPA+Pred (%)	78 (94.0)	366 (95.3)	0.620
CsA+MPA+Pred (%)	5 (6.0)	18 (4.7)	



# RESULTS

**Table 2.** Pre-transplant HBV serology in the two groups

	D(HBsAg+)/R(HBsAg-) group (n=83)	D(HBcAb+)/R(HBcAb-) group (n=384)	P value
<b>Donors' pre-transplant HBV serology</b>			
HBsAg+	83 (100%)	0	<b>&lt;0.001</b>
<1000 IU/ml	35 (42.2%)	0	/
≥1000 IU/ml	48 (57.8%)	0	/
HBsAb+	3 (3.6%)	283 (73.7%)	<b>&lt;0.001</b>
HBeAg+	0	0	/
HBeAb+	78 (94.0%)	146 (38.0%)	<b>&lt;0.001</b>
HBcAb+	82 (98.8%)	384 (100%)	0.178
HBV DNA+	24 (28.9%)	Unknown*	/
<b>Recipients' pre-transplant HBV serology</b>			
HBsAg+	0	0	/
HBsAb+	63 (75.9%)	153 (39.8%)	<b>&lt;0.001</b>
Titer 10-100 IU/L	31 (37.3%)	71 (18.5%)	
Titer > 100 IU/L	32 (38.6%)	82 (21.4%)	<b>0.001</b>
HBeAg+	0	0	/
HBeAb+	34 (41.0%)	1 (0.3%)	<b>&lt;0.001</b>
HBcAb+	58 (69.9%)	0	<b>&lt;0.001</b>
HBV DNA+	0	Unknown*	/

- **Median DNA level:**  $1.20 \times 10^3$  IU/ml (range  $5.86 \times 10 - 4.04 \times 10^6$ )
- **The donors:** HBsAg+, HBeAb+, HBcAb+ (77 donors, 92.8%), and 22/77 (28.6%) were HBV DNA+; **the recipients:** HBsAb+, HBeAb+, HBcAb+ (27 recipients, 32.5%)
- **No** HBV prophylaxis in the D(HBcAb+)/R(HBcAb-) group, whereas **all** D(HBsAg+)/R(HBsAg-) recipients received prophylaxis: HBIG alone (18, 21.7%), antiviral alone (41, 49.4%), combined (24, 28.9%).

## Median followup: **36 months**

**Table 3.** Post-transplant HBV serology in the two groups

	D(HBsAg+)/R(HBsAg-) group (n=83)	D(HBcAb+)/R(HBcAb-) group (n=384)	P value
Recipients' most recent HBV serology			
HBV DNA -->+	2 <sup>#</sup> (2.4%)	1 <sup>§</sup> (0.3%)	0.083
HBsAg -->+	2 <sup>#</sup> (2.4%)	1 <sup>§</sup> (0.3%)	0.083
HBeAg -->+	1 (1.2%)	1 (0.3%)	0.324
HBeAb -->+	4 (4.8%)	0	<b>0.001</b>
HBeAb +->-	4 (4.8%)	1 (0.3%)	<b>0.004</b>
HBcAb -->+	7 (8.4%)	10 (2.6%)	<b>0.019</b>
HBsAb titer downgrade	1 (1.2%)	29 (7.6%)	<b>0.027</b>
HBsAb titer upgrade	13 (15.7%)	15 (3.9%)	<b>0.002</b>





**Table 4.** Univariate analyses of potential pre-transplant donor and recipient risk factors influencing transplant outcomes in the D(HBsAg+)/R(HBsAg-) group

	HBsAg-→+		HBV DNA-→+		HBcAb -→+		Active liver injury		Graft loss		Death	
	Events	P value	Events	P value	Events	P value	Events	P value	Events	P value	Events	P value
<b>Donors' pre-transplant HBV factors</b>												
<b>HBsAg level</b>												
<1000 IU/ml (n=35)	1(2.9%)	1.000	1(2.9%)	1.000	4(11%)	0.448	2(5.7%)	0.458	1(2.9%)	0.635	3(8.6%)	0.646
≥1000 IU/ml (n=48)	1(2.1%)		1(2.1%)		3(6.3%)		6(13%)		3(6.3%)		2(4.2%)	
<b>HBV DNA</b>												
- (n=59)	1(1.7%)	0.497	1(1.7%)	0.497	4(6.8%)	0.407	4(6.8%)	0.220	2(6.7%)	0.575	3(5.1%)	0.624
+ (n=24)	1(4.2%)		1(4.2%)		3(13%)		4(17%)		2(6.7%)		2(6.7%)	
<b>Recipients' pre-transplant factors</b>												
<b>Age</b>												
≤40 yr (n=66)	2(3.0%)	1.000	2(3.0%)	1.000	6(9.1%)	1.000	7(11%)	1.000	3(4.5%)	1.000	5(7.6%)	0.578
>40 yr(n=17)	0		0		1(5.9%)		1(5.9%)		1(5.9%)		0	
<b>Gender</b>												
Male (n=64)	2(3.1%)	1.000	2(3.1%)	1.000	6(9.4%)	1.000	8(13%)	0.188	4(6.3%)	0.569	5(7.8%)	0.584
Female (n=19)	0		0		1(5.3%)		0		0		0	
<b>HLA mismatch</b>												
≤4 (n=68)	2(2.9%)	1.000	2(2.9%)	1.000	6(8.8%)	1.000	7(10%)	1.000	2(2.9%)	0.148	4(5.9%)	1.000
>4 (n=15)	0		0		1(6.7%)		1(6.7%)		2(13%)		1(6.7%)	
<b>HBsAb</b>												
- (n=20)	2(10%)	0.056*	2(10%)	0.056*	2(10%)	0.673*	4(20%)	0.091*	2(10%)	0.244*	3(15%)	0.088*
+ (n=63)	0		0		5(7.9%)		4(6.3%)		2(3.2%)		2(3.2%)	
10-100 IU/L (n=31)	0	0.056 <sup>#</sup>	0	0.056 <sup>#</sup>	3(9.7%)	0.785 <sup>#</sup>	1(3.2%)	0.157 <sup>#</sup>	2(6.5%)	0.168 <sup>#</sup>	1(3.2%)	0.241 <sup>#</sup>
>100 IU/L (n=32)	0		0		2(6.3%)		3(9.4%)		0		1(3.1%)	
<b>HBcAb</b>												
- (n=25)	2(8.0%)	0.088	2(8.0%)	0.088	7(28%)	/	4(16%)	0.234	1(4.0%)	1.000	3(12%)	0.158
+ (n=58)	0		0		0		4(6.9%)		3(5.2%)		2(3.4%)	
<b>HBsAb/HBcAb</b>												
+/+ (n=49)	0	<b>0.027</b>	0	<b>0.027</b>	0	/	3(6.1%)	0.149	2(4.1%)	0.365	2(4.1%)	<b>0.046</b>
+/- (n=14)	0		0		5(36%)	0.407 <sup>s</sup>	1(7.1%)		0		0	
-/+ (n=9)	0		0		0		1(11%)		1(11%)		0	
-/- (n=11)	2(18%)		2(18%)		2(18%)		3(27%)		1(9.1%)		3(27%)	
<b>HBV prophylaxis</b>												
<b>HBIG</b>												
Yes (n=42)	1(2.4%)	1.000	1(2.4%)	1.000	4(9.5%)	1.000	5(12%)	0.713	2(4.8%)	1.000	3(7.1%)	1.000
No (n=41)	1(2.4%)		1(2.4%)		3(7.3%)		3(7.3%)		2(4.9%)		2(4.9%)	
<b>Antiviral</b>												
Yes (n=65)	2(3.1%)	1.000	2(3.1%)	1.000	6(9.2%)	1.000	7(11%)	0.680	4(6.2%)	0.572	4(6.2%)	1.000
No (n=18)	0		0		1(5.6%)		1(5.6%)		0		1(5.6%)	

# CONCLUSIONS

Living D(HBsAg+)/R(HBsAg-) KTx in HBsAb+ recipients provides excellent graft and patient survivals without HBV transmission.

HBV transmission risks should be more balanced with respect to benefits of D(HBsAg+)/R(HBsAg-) KTx in HBsAb-/HBcAb- candidates.

