



Effects of antiviral therapy and drug withdrawal on postpartum hepatitis in pregnant women with chronic HBV infection

Minghui Li^{1,2} · Fangfang Sun¹ · Xiaoyue Bi¹ · Yanjie Lin² · Liu Yang¹ · Tingting Jiang¹ · Wen Deng¹ · Yao Lu¹ · Lu Zhang¹ · Wei Yi³ · Yao Xie^{1,2}

Received: 3 June 2022 / Accepted: 13 August 2022
© Asian Pacific Association for the Study of the Liver 2022

Abstract

Objective To explore the effects of antiviral therapy and drug withdrawal on postpartum hepatitis in pregnant women with chronic HBV infection (CHB) and decompensated liver disease (DL).
Methods Eligible CHB and DL pregnant women were divided into two groups: antiviral therapy group (n=32) and drug withdrawal group (n=24).
Results A total of 264 pregnant women were included, including 96 CHB and 168 DL. The incidence of postpartum hepatitis was 28.1% (27/96) in the antiviral therapy group and 23.7% (31/131) in the drug withdrawal group. The difference was not significant ($\chi^2=0.607, p=0.738$). No significant difference was observed in the incidence of postpartum hepatitis between the two groups (96.3% vs. 92.3%).
Conclusion Antiviral therapy and drug withdrawal had no significant effect on the incidence of postpartum hepatitis in pregnant women with CHB. Clinical trial registration number: NC 03214302.

Keywords Antiviral therapy · Hepatitis B virus · Maternal · Postpartum hepatitis

Introduction

Hepatitis B virus (HBV) is a global health problem. The prevalence of HBV infection is 1.4% in China, with a total of 28 million carriers. HBV infection is a major cause of liver disease and liver cancer.

HBV infection is a global health problem. The prevalence of HBV infection is 1.4% in China, with a total of 28 million carriers. HBV infection is a major cause of liver disease and liver cancer. In 2020, the incidence of HBV infection was 84%–92%. HBV infection is a major cause of liver disease and liver cancer. The incidence of HBV infection is 330,000 cases per year. HBV infection is a major cause of liver disease and liver cancer. The incidence of HBV infection is 5.7%. HBV infection is a major cause of liver disease and liver cancer. The incidence of HBV infection is 5.8–10%. HBV infection is a major cause of liver disease and liver cancer. The incidence of HBV infection is 4.1–10%.

✉ Yao Xie
xieyao1215@163.com

✉ Yao Lu
lu_yao00120184@foxmail.com

¹ Department of Hepatology, Dalian City Second Hospital, Dalian, China
Hospital, Central Medical University, Dalian 100015, China

² Department of Hepatology, Dalian City Second Hospital, Dalian, China
Hospital, Dalian, China

³ Department of Gastroenterology, Dalian City Second Hospital, Dalian, China
Hospital, Central Medical University, Dalian 100015, China



... a m a l e a a a i a l e a ...
 ... e e a a a a a a a a a i . A e i i -
 ... a l e i i a i a i e e H R i c i a
 ... a m a a l i , i a i i i i i i
 ... 50% 11, c a l l i i 6 m a l i 12,
 ... a m a i i i e e a a i B
 ... a l i a l 13. O i i i f i i i a
 ... H R DNA i i i a l i a a m a b i
 ... a m i a a (A L) i a i e e H R i c i
 ... a i i a i a l a a i e e
 ... e a i e e a a B 14. H
 ... e e e a i e e a a B
 ... - m a i a l a i i a m i
 ... e H R i c i a i l i m i i a a l
 ... a i a l a a l i i a e e e
 ... a m a e l a . I
 ... i e e a m a a i a m
 ... i e e H R i c i a a i i i
 ... a i a l a a i i m a c i
 ... i m i a i a l a m i e e e
 ... a l i .
 ... m i e e a m
 ... a i a i e e H R i c i e i
 ... e e a i a l a i a e
 ... - e i a n i i H R 15 19. I
 ... i e i m i a m e i a i
 ... a m a m m i i e l m
 ... a m a 15 19. a l a a m l
 ... e i i 2018. i a a m a l a a l
 ... l i e i e m m i i - H R i c a
 ... H R i c a m a a m a l l i e
 ... i i H R i c a m e e i i i i a l
 ... l a a a 10⁶ I / m l 14. C
 ... e e e a i e e a
 ... m a l i a m i e e H R i c
 ... i . I e i i e e e
 ... a m a i a a m i
 ... e H R i c i a m i e i D F
 ... a m i m - e i a n i i
 ... H R i a c a a m i m m i
 ... a l a l i 6 a l i
 ... i l m a c e a l a l e D F a m a
 ... i a a l i a e e e
 ... a m a a .

... a a l a m i a l i a B i i D i a H
 ... a l J a a 1, 2017 a D e m 30, 2019
 ... W . a a E C m m i
 ... B i i D i a H i a l A l a C a i a l i i
 ... M e a l e i e (J i D i L K i 2017 N . 004-02), a
 ... i C l i e a l (N C 03214302).
 ... I e i e i a : H B A i i a H R DNA
 ... > 10⁶ I / m l ; N a i H R
 ... ; N a e i e i i , m
 ... m m a , a a l i a

Patients and methods

Subjects and study design

... a e i a i a l e H B A -
 ... i i a H R - D N A i i a m . E l i t
 ... m i e e H R i c i a



HBV DNA level $> 10^5$ IU/ml. HBV DNA level $> 10^5$ IU/ml was observed in 500 (36.4%) of the 1372 pregnant women. HBV DNA level $< 10^5$ IU/ml was observed in 872 (63.6%) of the 1372 pregnant women.

Statistical analysis

The statistical analysis was performed using the SPSS 17.0 software package. The chi-square test was used to compare the categorical variables. The Fisher's exact test was used for the comparison of the categorical variables with small cell counts. The Mann-Whitney U test was used for the comparison of the continuous variables. The results were considered statistically significant when $p < 0.05$.

Results

Patient enrollment and deposition

A total of 397 HBV DNA-positive pregnant women were enrolled in the study. The mean age was 30.74 ± 3.85 years. The mean gestational week at enrollment was 32.12 weeks. The mean gestational week at delivery was 37.24 weeks. The mean gestational week at enrollment was significantly lower than the mean gestational week at delivery ($p < 0.001$). The mean gestational week at enrollment was significantly lower than the mean gestational week at delivery ($p < 0.001$). The mean gestational week at enrollment was significantly lower than the mean gestational week at delivery ($p < 0.001$).

Changes of biochemical indexes and HBV DNA during pregnancy

The changes of biochemical indexes and HBV DNA during pregnancy are shown in Table 1.

The mean gestational week at enrollment was significantly lower than the mean gestational week at delivery ($p < 0.001$).

Changes of HBV DNA content during pregnancy and after delivery

A total of 264 HBV DNA-positive pregnant women were enrolled in the study. The mean gestational week at enrollment was 32.12 weeks. The mean gestational week at delivery was 37.24 weeks. The mean gestational week at enrollment was significantly lower than the mean gestational week at delivery ($p < 0.001$).

Occurrence of postpartum hepatitis and treatment

A total of 67 HBV DNA-positive pregnant women were enrolled in the study. The mean gestational week at enrollment was 32.12 weeks. The mean gestational week at delivery was 37.24 weeks. The mean gestational week at enrollment was significantly lower than the mean gestational week at delivery ($p < 0.001$).

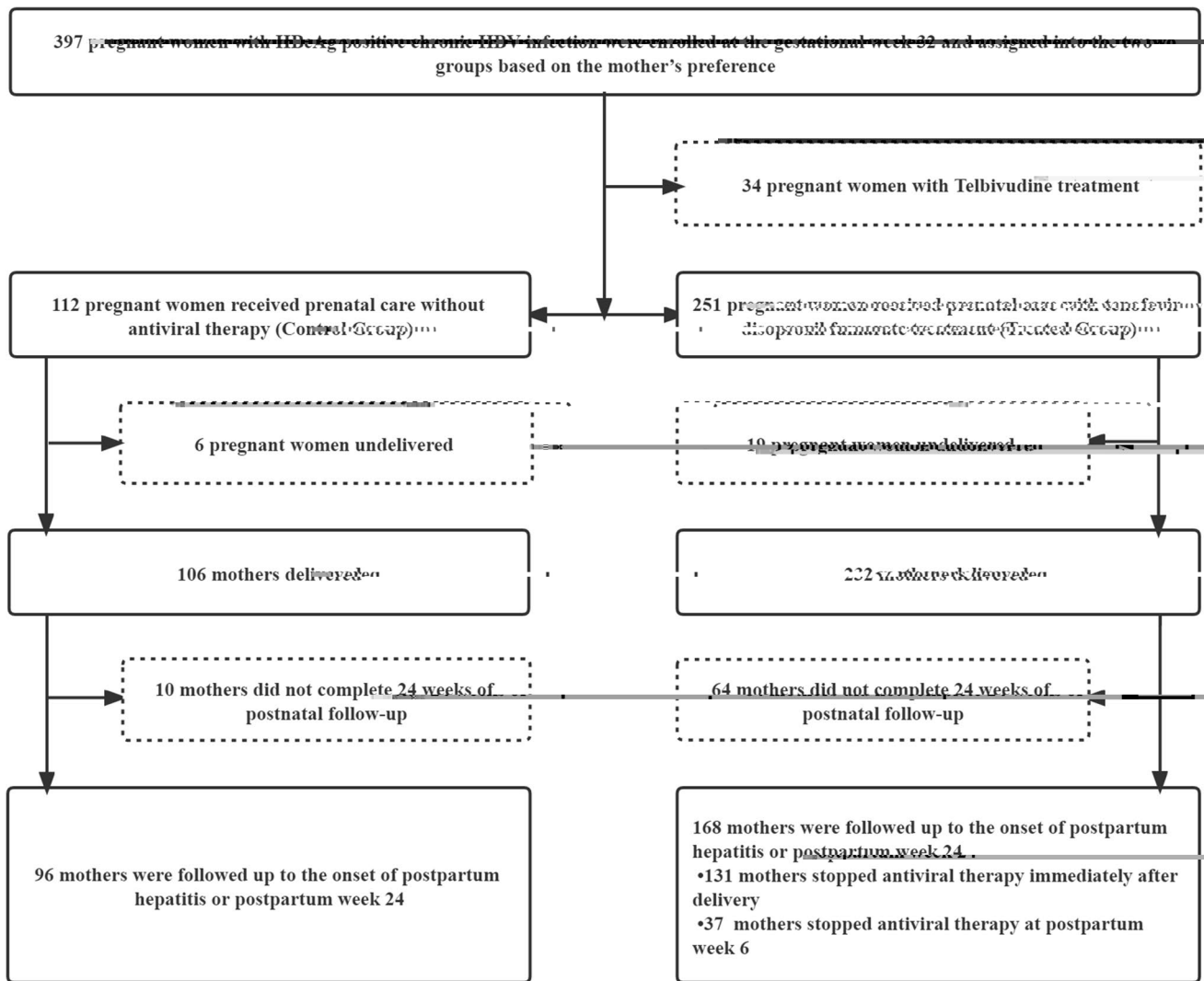


Fig. 1 Study design and participant flow

28. EG-IFN treatment significantly reduced the levels of HBV DNA in the blood of newborns compared with the control group (P < 0.05).

HBV markers at birth and blocking effect of HBV mother-to-child transmission in newborns

At birth, 346 newborns (96.3%) were positive for HBsAg, 189 (54.6%) were positive for HBeAg, and 157 (45.4%) were positive for HBV DNA. The mean levels of HBsAg, HBeAg, and HBV DNA were 3311.78 IU/mL, 424.04 IU/mL, and 9.97 IU/mL, respectively.

At birth, 168 newborns (73.1%) were positive for HBsAg, 100 (59.5%) were positive for HBeAg, and 100 (59.5%) were positive for HBV DNA. The mean levels of HBsAg, HBeAg, and HBV DNA were 10.00 IU/mL, 0.22 IU/mL, and 0.00 IU/mL, respectively. The difference in the levels of HBV markers between the two groups was statistically significant (P < 0.05). The mean levels of HBsAg, HBeAg, and HBV DNA in the newborns of the control group were significantly higher than those in the newborns of the treatment group (P < 0.05).

Table 1 Clinical laboratory investigations

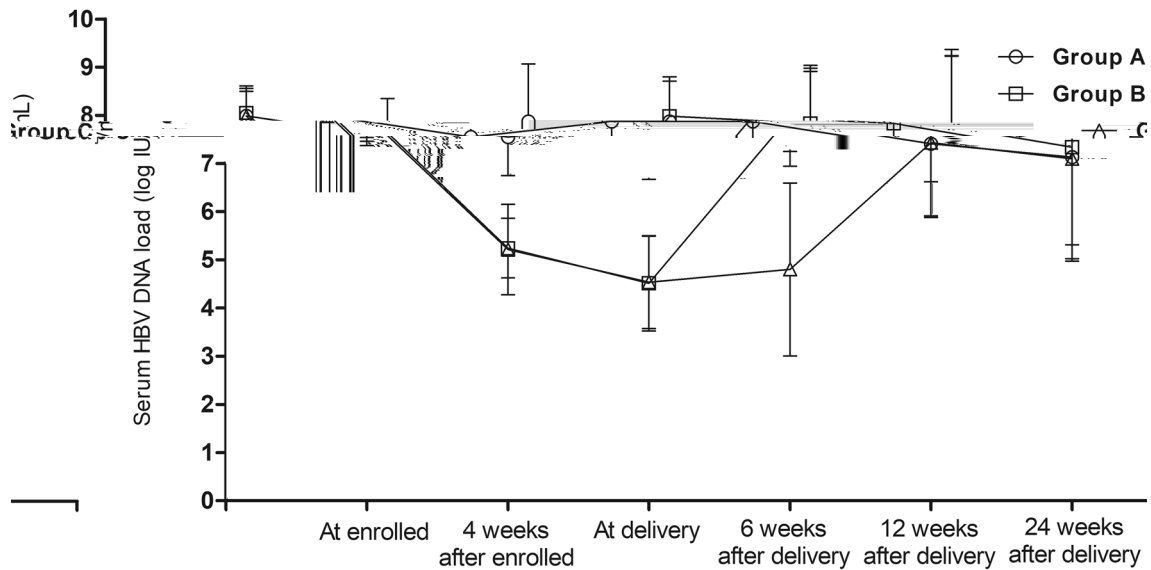
	Case	Control	P-value	Case	Control	P-value	Case	Control	P-value
A (g)	29.99	31.35	3.95	2.805	0.005	/	/	/	/
HBV DNA (10 IU/mL)	7.99	0.62		0.676	0.500	7.55	0.80	5.20	0.72
HBsAg (%)	100%	100%		100%	100%	100%	100%	100%	100%
AL (g/L)	22.17	14.80	23.46	20.03	0.051	0.960	20.71	27.69	23.75
A (g/L)	21.60	14.61	22.44	6.21	0.239	0.812	20.85	13.03	23.63
BIL (umol/L)	7.11	2.41	7.74	2.59	1.909	0.057	7.62	3.44	7.99
DBIL (umol/L)	1.72	0.76	1.771	2.23	0.157	0.875	1.70	1.03	1.91
ALB (g/L)	39.03	3.28	37.09	2.07	5.525	<0.001	36.75	2.44	36.24
GGT (U/L)	10.15	7.81	9.60	6.73	0.957	0.339	9.79	6.77	9.37
AL (U/L)	70.55	34.25	76.80	23.13	1.600	0.112	129.88	52.41	149.66
BA (umol/L)	3.25	2.60	4.11	8.91	0.531	0.596	3.70	3.35	7.66
BUN (umol/L)	3.08	0.78	3.96	11.64	0.662	0.509	2.92	0.62	3.10
C (umol/L)	44.33	5.78	45.63	11.95	0.530	0.597	46.67	5.19	50.90
HO (umol/L)	1.11	0.10	1.18	0.65	0.865	0.388	1.15	0.13	1.13
A (%)	109.99	13.45	113.40	10.34	2.089	0.041	116.68	9.95	116.79
IN	0.97	0.05	1.35	6.0	3.7990	0.605	3.98	2.1	6.9840

No es: HBV DNA; ALB: Albumin; BIL: Bilirubin; DBIL: Direct Bilirubin; AL: Aspartate Aminotransferase; BA: Bile Acids; BUN: Blood Urea Nitrogen; A: Alanine Aminotransferase; HO: Hemoglobin; IN: International Normalized Ratio; EMC: Enzyme-Linked Immunosorbent Assay

Table 2. HBV DNA load (log IU/mL) at different time points in Group A and Group B.

Time point	Group A (log IU/mL)	Group B (log IU/mL)	Median (IQR)	P-value
Baseline	7.99 (0.62, 8.05)	7.98 (0.52, 0.708/0.479)	0.077/0.939	0.648/0.518
4 weeks	7.55 (0.80, 5.24)	5.21 (0.94, 11.226/<0.001)	6.966/<0.001	0.207/0.837
6 weeks	7.87 (1.20, 4.51)	4.53 (0.96, 22.875/<0.001)	15.275/<0.001	0.016/0.987
12 weeks	7.87 (0.93, 7.98)	4.80 (1.79, 0.866/0.388)	9.339/<0.001	10.212/<0.001
24 weeks	7.41 (1.50, 7.83)	7.43 (1.55, 1.276/0.211)	0.049/0.961	1.336/0.184
24 weeks (Group B only)	7.13 (2.11, 7.34)	7.10 (2.13, 0.535/0.593)	0.056/0.956	0.476/0.635

Notes: C: Control; I: Initial; A: Antiviral; D: Delivery; T: Treatment; P: Postnatal; C: Control; D: Delivery; T: Treatment; P: Postnatal; I: Initial; A: Antiviral.



Group A: women untreated with antiviral drugs during pregnancy
 Group B: women with withdrawal antiviral drugs at delivery
 Group C: women with withdrawal antiviral drugs at 6 weeks after delivery

Fig. 2. Change in HBV DNA load (log IU/mL) over time in Group A and Group B.

All women in Group A (HBIG 100 IU/kg at 10, 20, and 30 weeks) and Group B (HBIG 100 IU/kg at 10, 20, and 30 weeks) had a significant reduction in HBV DNA load at 4 weeks (155/156, 99.35%) and at 24 weeks (96/106, 90.56%) ($\chi^2=12.132, p < 0.001$).

Discussion

Group A women who were not treated with antiviral drugs during pregnancy had a significant reduction in HBV DNA load at 4 weeks (155/156, 99.35%) and at 24 weeks (96/106, 90.56%) ($\chi^2=12.132, p < 0.001$).

Table 3 I s i e c e

	$\chi^2(p.a.l)$	$\chi^2(p.a.l)$	$\chi^2(p.a.l)$	$\chi^2(p.a.l)$	$\chi^2(p.a.l)$
C	0.601/0.438	0.007/0.934	0.195/0.658	0.580/0.446	24.3% (9)
I s i e c e	0.601/0.438	0.007/0.934	0.195/0.658	0.580/0.446	23.7% (31)
(n)					28.1% (27)

N : C
 Lmm a
 D b a

W i a W a l
 a W m W i c e
 A i i a l
 i m
 H R
 W i i f e a
 a e m e c i a i a l
 W e l
 a i m
 20, 21,
 24, 25 . C
 a i i a l
 c
 a a i i a l
 e d a n n i
 H R
 20, 21, 24, 25
 a i m
 D F
 a l i
 a i l m i
 W m
 i D F
 H R
 i i a c
 H R
 W i i f e a
 a e c l
 M a
 a e c m l e a i
 i) a
 l i e m l e a i
 a m m
 a)
 D F
 a a l a
 i a i
 a i i a l
 i
 m m a
 a a l l i a
 a c a /
 l i e m
 l e a i
 e l
 a i
 e a
 l i
 l i f
 a c i
 a
 e l
 A
 a c i
 c a l l
 a l i m a i m
 W e l l m i
 i D F a i i a l
 D F
 e m m
 f e e
 i
 m
 e d a n n i
 H R
 e a i c a
 i l i i i
 H R
 l e a i
 W i l i l
 a c a
 i a
 a e
 25, 26
 a
 W a
 a a l i m m i a i
 i
 H R
 D N A
 a
 W m
 e
 10⁶ I / m l
 l i
 m
 e d a n n i
 H R
 e l
 c i l l e
 27 30
 m
 i
 e m m
 a i i a l
 a
 a e
 l e i
 m
 e d a n n i
 H R
 i
 a
 W m
 W i
 H R
 D N A < 10⁶ I / m l
 31 . A l
 m
 e
 i l i
 e m m
 a i i a l
 a
 i
 m
 e d a n n i
 H R
 m 28
 a i
 D F e a
 e H R
 D N A
 m
 a 31
 (H R
 D N A < 10⁶ I / m l)
 i
 a
 W m
 a 4
 a
 m
 i i i i
 l e a i
 32
 m i m i
 a l
 D F a
 e
 i
 i
 a
 W m
 a i i a l
 a
 a 32
 W
 a i i
 O
 a
 a
 e c c
 a
 m
 e d l e i
 i
 a 32
 W
 a i
 99.35%
 W e
 i f e a
 l i
 a
 a i
 C
 (90.56%)
 A
 a
 m
 i m
 H R
 D N A

... a c, HBV DNA... li a ...
im... a... a...
I e e... a... a... a... m... im... t...
a... a... 6... a... li... i... a... e... i... c...
... a... a... li... A... 90%... a... b... e...
... i... 12... a... li... i... a... i... a... i... a... l...
... a... m... a... imm... i... l... a... i... a... l... a... m...
... a... li... D... l... a... i... a... m... i... l... a...
... a... m... a... O... a... a... a... a... a... a...
... a... m... 12... a... a... a... a... a... a... a...
... a... i... m... i... e... e... e... a...
H... ,... m... e... m... l... a... a...
... a... m... ,... e... e... i...
... a... m... ,... e... m... i... i... l... 24...
... a... li... na... l... i... c... i... e... b... a... a...
... e... m... i... c... i... e... e... a... a... 48
... a... m... i...

Acknowledgements

... a 6(12 1/A° al ()>>BBDC() .76 (. -MC8.687 .805 (. a)5997(a M,)5997(a 7)741809(6948(F)-2

20. C... I... D... CMA, C...
H... CMA...
... B... Ga... Bi...
2019;2019(27):938-961
21. ... NA, B... NH, C... KM, H... J, J... MM,
M... MH, A... A... Li D.
AA LD... B.H...
2016;63:261-283.
22. ... HH, L... HF, C... C... B... (HR...)
... H... 2008;2:370-375
23. C... J, L... L... H... M... Fa...
... mi... mi...
... B.F... M (La...)
2021;8: 796901
24. ... K, K... M, La... GK, A... C... HL, C... CJ, al.
... 2015... H... 2016;10:1-98
25. E... A... Li... E...
... EA L.
... G... B...
... JH... 2017;2017(67):370-398
26. ... H... Ga... Bi...
2016;24:881-884
27. L... FC, Li J, ... J, C... JY... L, al...
...
... C... 2017;35:6627-6633
28. Li J, ... B, C... C... J, F... J... C, al...
... B...
... Di Li D... 2019;51:864-869
29. C... K... M... Ka... A... D, K... KO... L,