بسم الله الرحمن الرحيم

Clinical significance of occult hepatitis B virus infection

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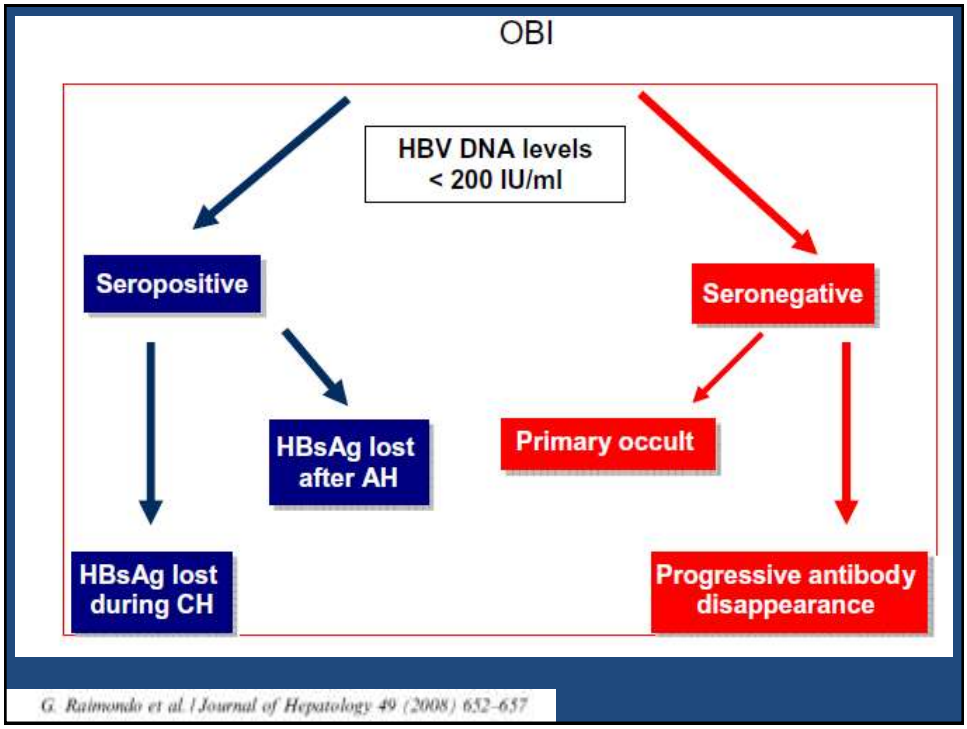
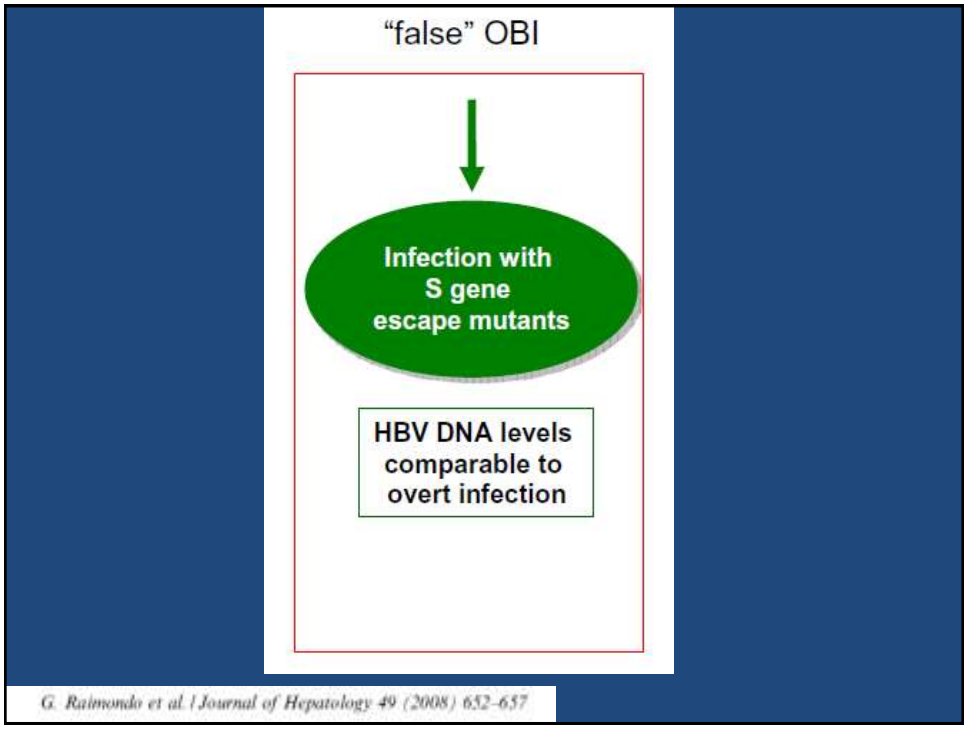
October 2016

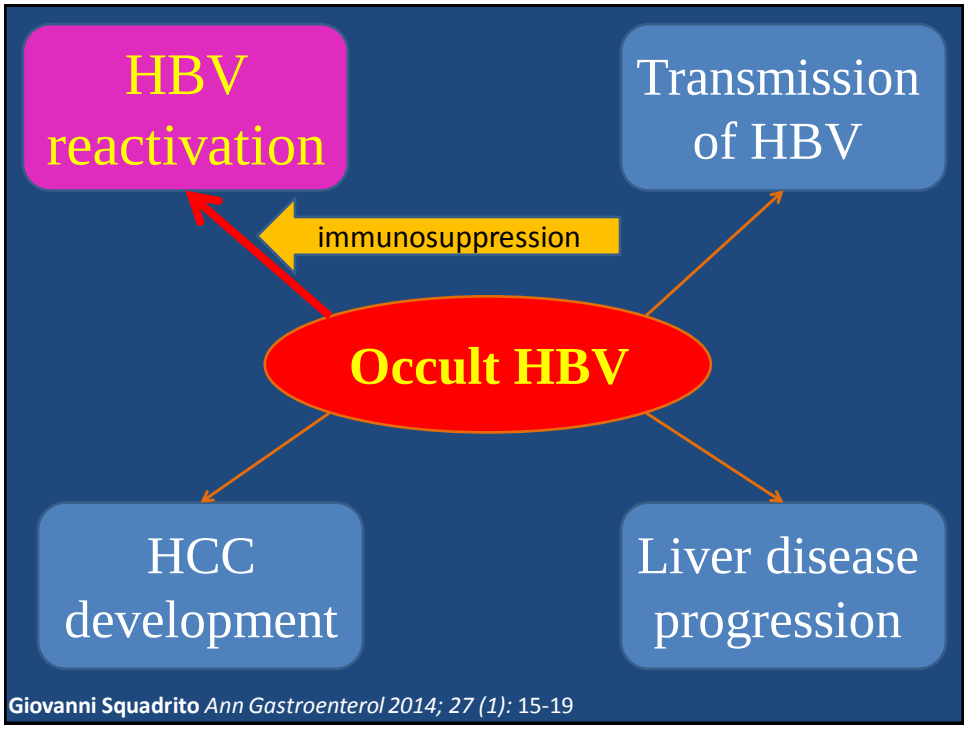
Occult hepatitis B virus infection (OBI)

- Presence of HBV DNA in the liver (with detectable or undetectable HBV DNA in the serum) & HBsAg negative
  - Seropositive-OBI
    - anti-HBc and/or anti-HBs positive
  - Seronegative-OBI
    - anti-HBc and anti-HBs negative

G. Raimondo et al. / Journal of Hepatology 49 (2008) 652–657


OBI
HBV DNA levels
< 200 IU/ml
Seropositive
Seronegative
HBsAg lost
after AH
Primary occult
HBsAg lost
during CH
Progressive antibody
disappearance
G. Raimondo et al. / Journal of Hepatology 49 (2008) 652–657


"false" OBI
Infection with
S gene
escape mutants
HBV DNA levels
comparable to
overt infection
G. Raimondo et al. / Journal of Hepatology 49 (2008) 652–657



Giovanni Squadrito *Ann Gastroenterol 2014; 27 (1):* 15-19

WJH 6th Anniversary Special Issues (3): Hepatitis B virus

Occult hepatitis B virus infection

- ***Transmission of OBI***
  - **–Transfusion:**
    - The infectivity of OBI by transfusion is determined
      - –Viral load / the volume of plasma
      - –HBV serological status (anti-HBc and/or anti- HBs)
        - » high anti-HBs levels → unlikely to transmit the infection
        - » anti-HBc only→ may transmit the infection

World J Hepatol 2014 December 27; 6(12): 860-869

WJH 6th Anniversary Special Issues (3): Hepatitis B virus

Occult hepatitis B virus infection

- ***Transmission of OBI***
  - **–Organ transplantation**
    - The transmission of HBV infection OBI donors to recipients → 17%-94%
      - –prophylaxis is recommended to prevent HBV reactivation
    - It is uncertain whether OBI is transmitted from HBV-seronegative donors

World J Hepatol 2014 December 27; 6(12): 860-869

WJH 6th Anniversary Special Issues (3): Hepatitis B virus

Occult hepatitis B virus infection

- ***Transmission of OBI***
  - **–Hemodialysis**
    - The prevalence of OBI in hemodialysis patients varies from 0% to 54%
    - Regular screening for HBV DNA with sensitive PCR-based assays in all dialysis patients

World J Hepatol 2014 December 27; 6(12): 860-869

- **Pregnancy and OBI transmission:**
  - 202 healthy pregnant women
  - 6 (3%) individuals were HBV DNA positive with TaqMan & COBAS Amplicor PCR methods
    - Cord blood was obtained from four of six individuals showed that all samples were HBV-DNA negative

Serial number	Age (year)	Height (cm)	Weight (kg)	HBV immunization history	HBsAg	HBsAb	HBcAb IgG	HCV Ab	HBV-DNA level: TaqMan method (copies/ml)	HBV-DNA level: COBAS test (copies/ml)
75	33	162	68	+	–	+	–	–	UDR	UDR
73	28	170	65	+	–	+	–	–	UDR	UDR
71	36	161	60	–	–	–	–	–	UDR	UDR
48	35	160	53	+	–	+	–	–	UDR	UDR

Kwon et al .Occult HBV infection in pregnant woman. Liver International (2008)

PLOS ONE

RESEARCH ARTICLE

Occult HBV Infection May Be Transmitted through Close Contact and Manifest as an Overt Infection

Li-Ping Hu[1,2], De-Ping Liu[3], Qin-Yan Chen[1], Tim J. Harrison[4], Xiang He[5], Xue-Yan Wang[1], Hai Li[1], Chao Tan[1], Qing-Li Yang[1], Kai-Wen Li[1,2], Zhong-Liao Fang[1]*

- The study subjects were a three member family, a boy and his parents

PLOS ONE , October 12, 2015

Samples	HBsAg	Anti-HBs	Anti-HBc	Viral loads
Father	-	-	+	8×10^5 IU/m
Mother	-	+	+	3.53×10^3 IU/
Son	+	-	+	5.42×10^5 IU/

PLOS ONE , October 12, 2015

Serotypes and genotypes predicted from the sequences from each study subject

Study subject	Number of clones	Serotypes	Genotypes
Father			
	9	adrq+	C2
	1	ayw1	B
	1	ayw	B
	1	ayr	Recombinant (B/C)
Total	12		
Mother			
	7	adwq+	C5
	1	ayw1	B
	1	ayw1	Recombinant (B/C)
	1	adw2	Recombinant (B/C)
	1	adwq+	Recombinant (C/G)
Total	11		
Son			
	9	adrq+	C2
Total	9		

- The son has one serotype (adrq+) & one genotype (C2) and this was seen in the father but not the mother.
- All of the sequences from the son have the same amino acid substitution pattern in the S protein as that seen in the father

- Strong evidence of transmission from father to son

PLOS ONE , October 12, 2015

OBI & chronic liver disease

Hepat Mon.2012;12(11):e7292. DOI: 10.5812/hepatmon.7292
KOWSAR
Hepatitis Monthly
www.HepatMon.com

Occult Hepatitis B Virus Infection in Patients With Chronic Hepatitis C Treated With Antiviral Therapy

Gian Paolo Caviglia [1], Maria Lorena Abate [1], Paola Manzini [2], Franca Danielle [2], Alessia Cian-

- 137 HBsAg-negative chronic hepatitis C
  - treated with pegylated-interferon and ribavirin
    - 73 Responders/74 Non Responders

Hepat Mon.2012;12(11):e7292. DOI: 10.5812/hepatmon.7292
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Gian Paolo Caviglia [1], Maria Lorena Abate [1], Paola Manzini [2], Franca Danielle [2], Alessia Cian-

Characteristic	All Patients	Liver Biopsy Subgroup
No. of patients	137	35

	All Patients	Liver Biopsy Subgroup
HBV markers positive, No. (%)	73 (53.3%)	19 (54.3%)
Anti-HBc positive	25 (18.3%)	7 (20%)
Anti-HBc/anti-HBs positive	24 (17.5%)	7 (20%)

Hepat Mon. 2012

Hepat Mon.2012;12(11):e7292. DOI: 10.5812/hepatmon.7292
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Table 3. Characteristics of Patients With Liver Biopsy (n = 35) According to OBI Status

	OBI positive	OBI negative	*P* value
No. of patients	13 (37.1%)	22 (62.9%)	
Sex (M/F)	10/3	12/10	0.282
Age, y, range	50.1 (31-68)	47.4 (29-66)	0.681
AST, IU/L, mean ± SD	82 ± 35	63 ± 32	0.112
ALT, IU/L, mean ± SD	136 ± 84	102 ± 64	0.183
Ishak histology fibrosis score, mean ± SD	2.69 ± 0.63	2.86 ±1.46	0.863
Ishak histology activity score, mean ± SD	4.69 ± 1.25	4.45 ± 2.22	0.483
HCV genotype 1, No. (%)	11 (85%)	17 (77%)	0.689
Basal HCV Viral load, IU/ml, median	2.0 × 106	1.6 × 106	0.441
Therapy outcome R vs. NR, % R	5 vs. 8 (38.5%)	7 vs. 15 (31.8%)	0.726

Hepat Mon. 2012

Hepat Mon.2012;12(11):e7292. DOI: 10.5812/hepatmon.7292
KOWSAR
Hepatitis Monthly
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Occult Hepatitis B Virus Infection in Patients With Chronic Hepatitis C Treated With Antiviral Therapy

Gian Paolo Caviglia [1], Maria Lorena Abate [1], Paola Manzini [2], Franca Danielle [2], Alessia Cian-

Conclusions: Despite the high prevalence rate of liver HBV DNA in patients with CHC SVR was not affected by occult HBV infection.

Jundishapur J Microbiol. 2015 March; 8(3): e16873. DOI: 10.5812/jjm.16873
Published online 2015 March 21. Research Article

Occult Hepatitis B Infection in Patients With Cryptogenic Liver Cirrhosis in Southwest of Iran

Seyed Jalal Hashemi [1,*]; Eskandar Hajiani [2]; Abdolrahim Masjedizadeh [2]; Manoochehr

- 50 patients with cryptogenic cirrhosis
- 80 healthy individual without any risk factors as a control group
- Their sera were tested for HBV DNA
-

Jundishapur J Microbiol. 2015 March; 8(3): e16873. DOI: 10.5812/jjm.16873
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Table 1. Etiologies of Liver Diseases Among the Studied Patients

Etiology of Liver Disease	Number of Cases
HBV infection	70 (42.4)
Autoimmune Hepatitis	23 (14)
HCV infection	15 (9.1)
Wilson's Disease	2 (1.2)
Cryptogenic	55 (33.3)

Jundishapur J Microbiol. 2015 March; 8(3): e16873. DOI: 10.5812/jjm.16873
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Table 2. Characteristics of Patients and Control Group[a, b]

Variable	Cryptogenic Cirrhosis (n = 50)	Healthy Control (n = 80)	P Value
Age, y	53.34 ± 14.73	32.65 ± 8.51	0.001
Male	36 (72)	27 (33.8)	0.001
ALT IU/L	39.48 ± 14.73	28.40 ± 11.85	0.005
AST IU/L	57.46 ± 25.93	24.55 ± 8.49	0.0001
HBcAb	10 (20)	8 (10)	0.100
HBsAb	12 (24)	18 (21)	0.843
OBI	7 (14)	0 (0)	0.001

Jundishapur J Microbiol. 2015 March; 8(3): e16873. DOI: 10.5812/jjm.16873
Published online 2015 March 21. Research Article

Occult Hepatitis B Infection in Patients With Cryptogenic Liver Cirrhosis in Southwest of Iran

Seyed Jalal Hashemi [1,*]; Eskandar Hajiani [2]; Abdolrahim Masjedizadeh [2]; Manoochehr

Table 3. Characteristics of Cirrhotic Patients With and Without Occult Hepatitis B Virus Infection[a]

Variable	HBV DNA-Positive (n = 7)[b]	HBV DNA-Negative (n = 43)[b]	P Value	95% Confidence Interv the Difference
Male	5 (71.2)	31 (72.1)	0.90	
Age, y	54.00 ± 8.386	8.386 ± 15.590	0.849	-11.42 to 12.96
ALT, IU/L	45.8571 33.363	38.441 ± 31.260	0.567	-18.423 to 9.265
AST, IU/L	73.8571 ± 46.8950	54.790 ± 20.438	0.071	-1.671 to 39.80
AlkP, IU/L	197.857 ± 9.940	218.488 ± 58.482	0.038	-40.092 to -1.170
Bilirubin	1.20 ± 0.472	1.353 ± 0.837	0.640	-0.809 to 0.503
Albumin	3.628 ± 0.419	3.630 ± 0.587	0.994	-0.468 to 0.464
PT, s	15.857 ± 2.1157	15.0605 ± 2.59396	0.395	-1.284 to 2.877
FBS, mg/dL	102.8571 ± 21.95	98.860 ± 23.442	0.675	-15.066 to 23.593
Cholesterol, mg/dL	200.714 ± 13.047	197.697 ± 12.279	0.553	-7.126 to 13.160
Time to decompensation, y	1.47 ± 1.283	4.327 ± 3.920	0.002	-4.585 to -1.230

Liver, Pancreas and Biliary Tract

Occult hepatitis B virus and the risk for chronic liver disease: A meta-analysis

Loredana Covolo[a,*], Teresa Pollicino[b], Giovanni Raimondo[b], Francesco Donato[a]

[a] Institute of Hygiene, Epidemiology and Public Health, University of Brescia, Brescia, Italy
[b] Department of Internal Medicine, Unit of Clinical and Molecular Hepatology, University Hospital of Messina, Messina, Italy

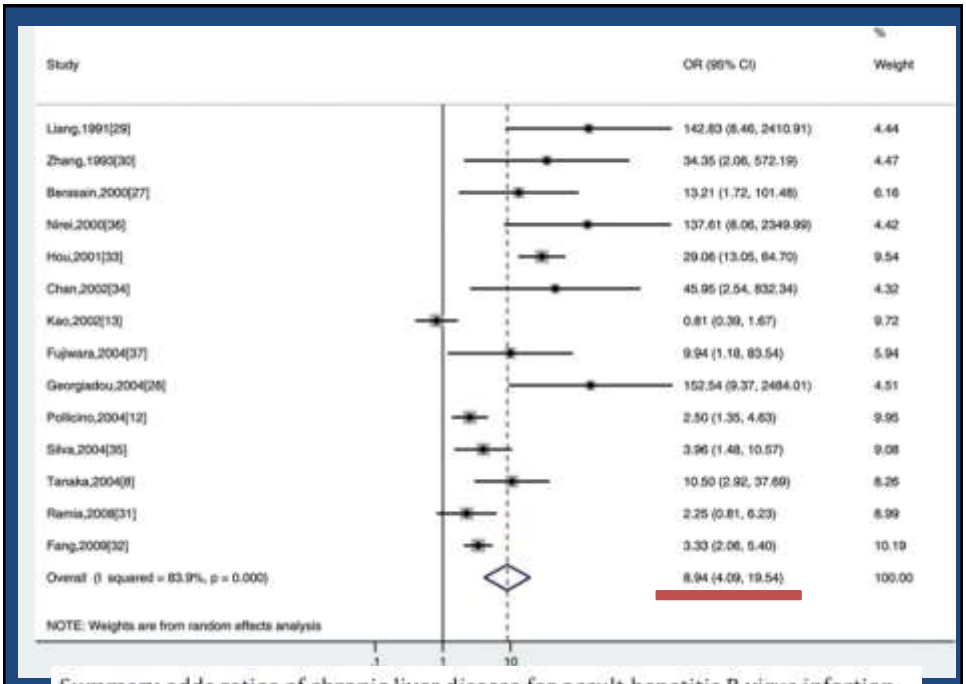
1168 records identified in Pub Med and EMBASE

↓

14 articles included in analysis

- A total of 1503 subjects with (cases) and 2052 without chronic liver disease (controls) were included.

L. Covolo et al. / Digestive and Liver Disease 45 (2013) 238– 244



Summary odds ratios of chronic liver disease for occult hepatitis B virus infection.

Liver, Pancreas and Biliary Tract

Occult hepatitis B virus and the risk for chronic liver disease: A meta-analysis

Loredana Covolo[a,*], Teresa Pollicino[b], Giovanni Raimondo[b], Francesco Donato[a]

[a] Institute of Hygiene, Epidemiology and Public Health, University of Brescia, Brescia, Italy
[b] Department of Internal Medicine, Unit of Clinical and Molecular Hepatology, University Hospital of Messina, Messina, Italy

Our findings show that OBI is associated with CLD, with an overall 8.9-fold increase in the risk as compared to individuals without the infection, thus suggesting a possible role of OBI also in CLD development.

L. Covolo et al. / Digestive and Liver Disease 45 (2013) 238– 244

OBI & Hepatocellular carcinoma

www.impactjournals.com/oncotarget/ July 28, 2016 Oncotarget, Vol. 7, No. 38

Clinical Research Paper

Occult HBV infection in HCC and cirrhotic tissue of HBsAg-negative patients: a virological and clinical study

- 68 patients ,biopsy proven cirrhosis and HCC

HCV: 85%
NASH:15%

Child-A Cirrhosis:85%
Child-B Cirrhosis: 15%

BCLC stage A: 90%
BCLC stage B: 8%
BCLC stage C: 2%

Mono Focal HCC:55%
Multi Focal HCC: 45%

www.impactjournals.com/oncotarget/ July 28, 2016 Oncotarget, Vol. 7, No. 38

Clinical Research Paper

Occult HBV infection in HCC and cirrhotic tissue of HBsAg-negative patients: a virological and clinical study

- OBI was observed in HCC tissue of
  - 20% of the 68 HBsAg-negative patients (13 patients)
  - 50 % of those with circulating anti-HBc alone
  - 30% of the anti-HBs/anti-HBc-positive
  - only 5% of the anti-HBc-negative
- significantly younger
- more advanced clinical condition (more severe Child-Pugh & worse BCLC score)

Parameters	Patients with occult HBV infection	Patients without occult HBV infection	*p*
N° of patients	13	55	
Mean age (±SD)	65.7 (8.0)	71.2 (5.3)	0.03*
Males, n° (%)	7 (53.8)	32 (58.2)	0.78**
Alcohol abusers(> 30g/die), n° (%)	1 (7.7)	1 (1.8)	0.26**
Subjects with diabetes, n° (%)	2 (15.4)	6 (10.9)	0.97**
BMI (mean ± SD)	28.8 (3.5)	26.6 (2.4)	0.07*
AST/ULN(mean ± SD)	1.85 (0.9)	1.64 (0.9)	0.52*
ALT/ULN (mean ± SD)	1.78 (1.0)	1.56 (0.8)	0.51*
ALP/ULN (mean ± SD)	1.38 (1.0)	1.12 (0.4)	0.41*
Total bilirubin, mg/dl (mean ± SD)	1.04 (0.5)	1.63 (4.0)	0.31*
PT% (mean ± SD)	92.8 (11.6)	83.1 (26.3)	0.06*
αfetoprotein, (mean ± SD)	97.5 (170.3)	188.9 (601.1)	0.39*
Anti-HCV-positive patients, n° (%) HCV-RNA-positive subjects, n° (%) HCV load, IU/mL (mean ± SD) with HCV-genotype 1, n° (%)	11 (84.6) 9 (81.8) 1.57E6 (2.48E6) 6 (54.5)	48 (85.4) 38 (79.2) 1.07E6 (1.64E6) 32 (68.1)	0.80** 0.99** 0.98* 0.23**
Patients with NASH, n°(%)	2 (15.4)	7 (12.7)	0.80**
Anti-HBs-negative/anti-HBc-positive, n° (%) Anti-HBs /anti-HBc-positive, n° (%) Anti-HBs /anti-HBc-negative, n° (%)	6 (46.1) 5 (38.5) 2 (15.4)	5 (9.1) 12 (21.8) 38 (69.1)	Anti-HBc pos vs neg <0.001**
Child Pugh score, n° (%): A B	6 (46.1) 7 (53.9)	52 (94.5) 3 (5.5)	<0.00001**
Patients with first diagnosis of HCC, n° (%)	8 (61.5)	40 (72.7)	
Patients with HCC relapse, n° (%)	5 (38.5)	15 (27.3)	0.45**
Patients with a single HCC, n° (%)	8 (61.5)	30 (54.6)	
Patients with multiple HCC, n° (%)	5 (38.5)	25 (45.4)	0.61**
Patients with portal thrombosis, n° (%)	1 (7.7)	1 (1.8)	0.26**
BCLC score, n° (%) of patients with Score A B C	 7 (53.9) 5 (38.5) 1 (7.6)	 54 (98.2) 1 (1.8) 0	Score A vs. B/C <0.00001**

www.impactjournals.com/oncotarget/ July 28, 2016 Oncotarget, Vol. 7, No. 38

Clinical Research Paper

Occult HBV infection in HCC and cirrhotic tissue of HBsAg-negative patients: a virological and clinical study

Conclusions: The study showed a significant correlation between OBI and the severity of liver damage

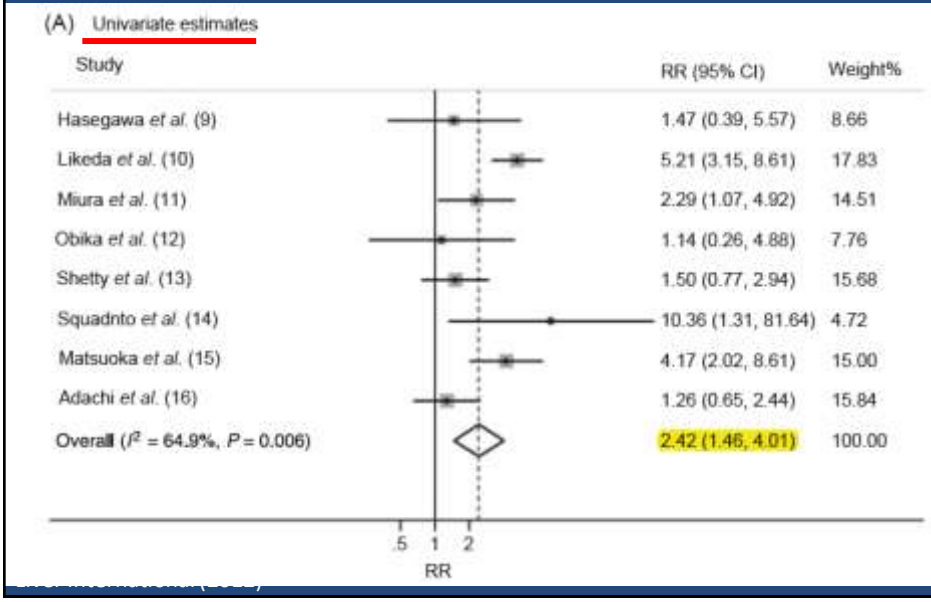
Liver INTERNATIONAL 2012
OFFICIAL JOURNAL OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE LIVER

Association between occult hepatitis B infection and the risk of hepatocellular carcinoma: a meta-analysis

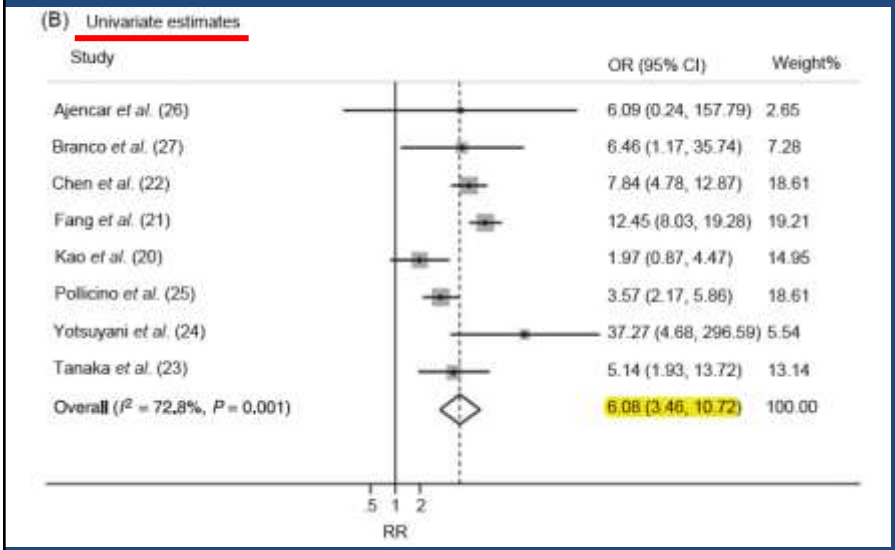
Yu Shi , Yi HuaWu , Wei Wu , Wan Jun Zhang , Jun Yang and Zhi Chen

- meta-analysis of prospective and retrospective studies
- from 1966 to 2010
- 16 eligible studies

Prospective studies: comparing the HCC risk in occult HBV individuals with that in those non-infected.

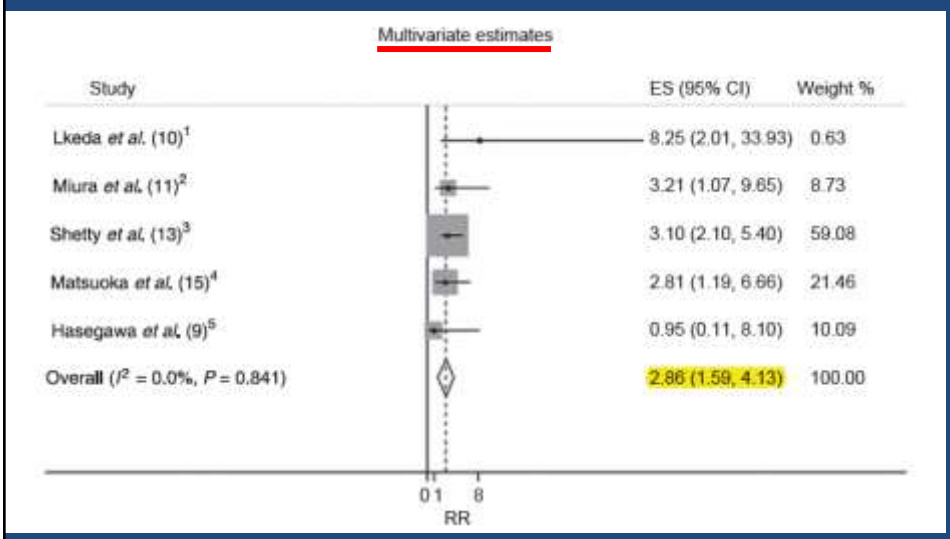


Retrospective studies: comparing the HCC risk in occult HBV individuals with that in those non-infected.



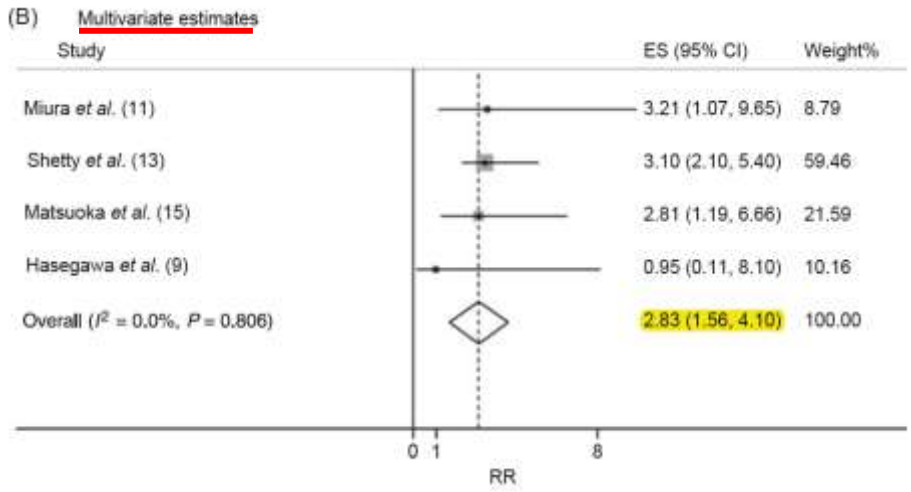
Liver International (2012)

Prospective studies : HCC risk in individuals with occult hepatitis B virus infection with that in those without infection



Liver International (2012)

longitudinal studies comparing HCC risk in occult hepatitis B virus and ***HCV-co-infected*** cases with that in those with HCV mono-infection



Liver International (2012)

Liver INTERNATIONAL

Clinical characteristics and potential aetiologies of non-B non-C hepatocellular carcinoma in hepatitis B virus endemic area

Seung Bum Lee, Kang Mo Kim, Jihyun An, Danbi Lee, Ju Hyun Shim, Young-Suk Lim, Han Chu Lee, Young-Hwa Chung and Yung Sang Lee

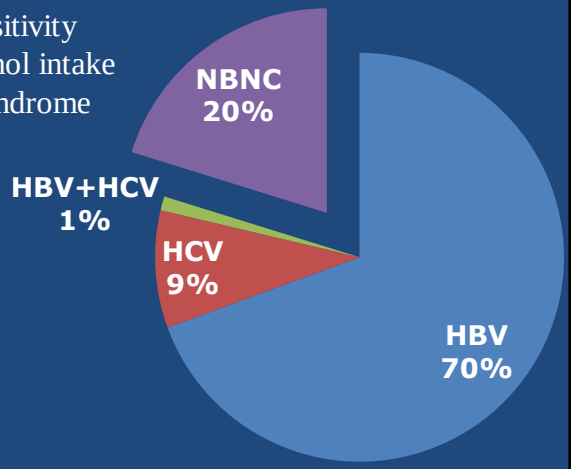
Department of Gastroenterology, Asan Liver Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Liver Int. 2016; 36: 1351–1361. DOI: 10.1111/liv.13099

- 4690 HCC patients
  - Asan Medical Center from 2007 to 2009.

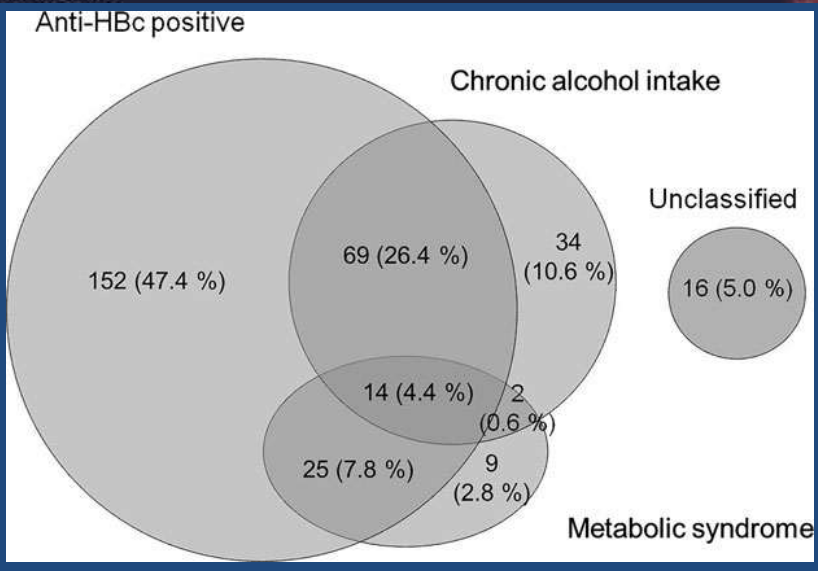
Liver INTERNATIONAL

- 523 NBNC HCC
  - Among 321 NBNC HCC patients whose hepatitis anti-HBc test results were available
    - 81.0% anti-HBc positivity
    - 37.1% chronic alcohol intake
    - 15.5% metabolic syndrome



Aetiology of 4960 patients with hepatocellular carcinoma

Liver INTERNATIONAL



Distribution of 321 patients with non-B non-C hepatocellular carcinoma whose result of hepatitis B virus core antibody IgG (anti-HBc) is available according to aetiologies.

Liver INTERNATIONAL

Characteristics	Multivariate analysis Hazard ratio (95% CI)	*P*-value
Age (years), ≥ 50 vs. < 50	–	–
Sex, male vs. female	–	–
Anti-HBc*, positive vs. negative	–	–
Chronic alcohol intake†, positive vs. negative	1.01 (0.78–1.32)	0.938
Metabolic syndrome‡, positive vs. negative	–	–
Underlying cirrhosis		
Child-Pugh class A vs. no evidence of cirrhosis	1.65 (1.17–2.34)	0.005
Child-Pugh class B/C vs. no evidence of cirrhosis	2.75 (1.86–4.06)	<0.001
AFP (ng/ml), ≥ 200 vs. < 200	1.47 (1.10–1.96)	0.009
Gross portal vein invasion, positive vs. negative	2.40 (1.53–3.76)	<0.001
Extrahepatic metastasis, positive vs. negative	1.55 (1.05–2.27)	0.026
ECOG PS		
1 vs. 0	1.53 (1.06–2.22)	0.024
2/3 vs. 0	7.99 (3.70–17.25)	<0.001
HCC stage, BCLC		
B vs. 0/A	2.74 (1.82–4.14)	<0.001
C/D vs. 0/A	3.36 (2.02–5.58)	<0.001

multivariate analysis of potential prognostic variables affecting the survival in 523 non-B non-C HCC

OBI and immunosupression

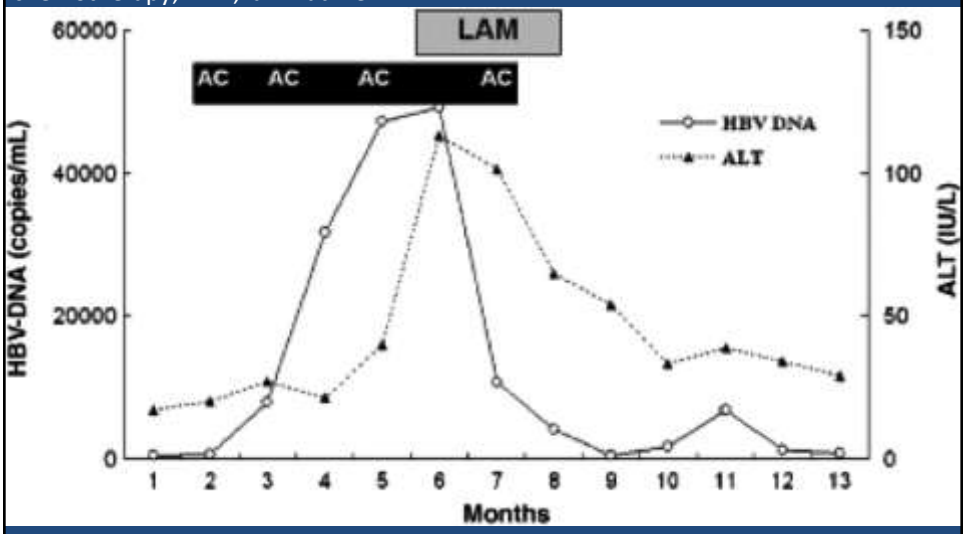
HBV reactivation

- Diagnosis of reactivation
  - –increase in HBV DNA
    - A detectable HBV DNA level when they previously had no virus present.
    - A rise in HBV DNA of more than 1-2 $\log_{10}$ IU/mL in patients who had HBV DNA present at baseline.

HBV FLARE

- A rise in transaminases with an ALT that is at least 3 to 5 times the baseline value +/- clinical signs and symptoms of hepatitis.
- Flares can occur at various times during the course of immunosuppressive therapy.
  - – while the patient is receiving immunosuppressive therapy
  - – after withdrawal of therapy (glucocorticoids, TNF-alpha inhibitors)

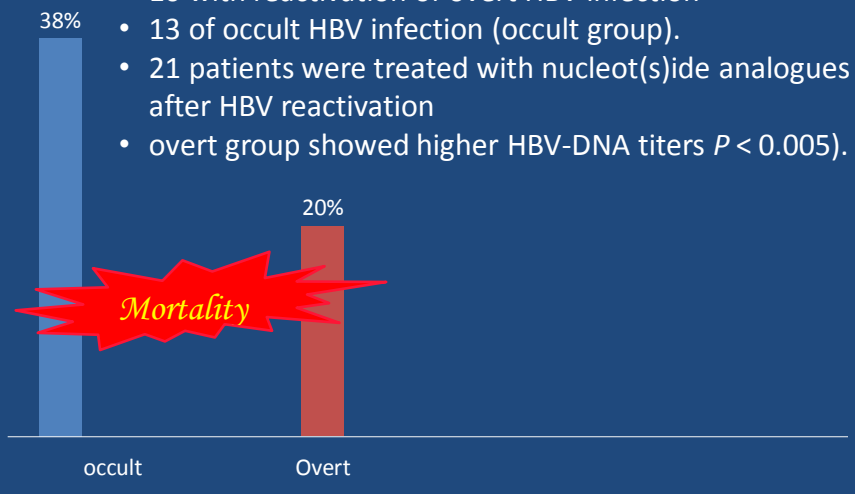
HBV reactivation in a breast cancer patient after 3 courses of chemotherapy and lamivudine was instituted for continuing chemotherapy. AC, administration of chemotherapy; LAM, lamivudine



Daniel Shouval, **Immunosuppression and HBV Reactivation** Semin Liver Dis 2013; 33(02):

HBV reactivation is life-threatening!!

- 23 patients with symptomatic HBV reactivation occurring during or after immunosuppressive
  - 10 with reactivation of overt HBV infection
  - 13 of occult HBV infection (occult group).
  - 21 patients were treated with nucleot(s)ide analogues after HBV reactivation
  - overt group showed higher HBV-DNA titers $P < 0.005$).



Nicola Coppola et al. J. Med. Virol. 83:1909–1916, 2011

Categorizing level of risk

- Patient's serologic status
- Type of immunosuppressive

Categorizing level of risk

- The high-risk group
  - HBVr in >10% of cases
    - AGA *recommends* screening for HBV
    - AGA *recommends* antiviral prophylaxis
- The moderate-risk group
  - HBVr 1-10% of cases
    - AGA *recommends* screening for HBV
    - The AGA *suggests* antiviral prophylaxis
- The low-risk group
  - HBVr <1% of cases
    - AGA *NOT recommends* screening for HBV

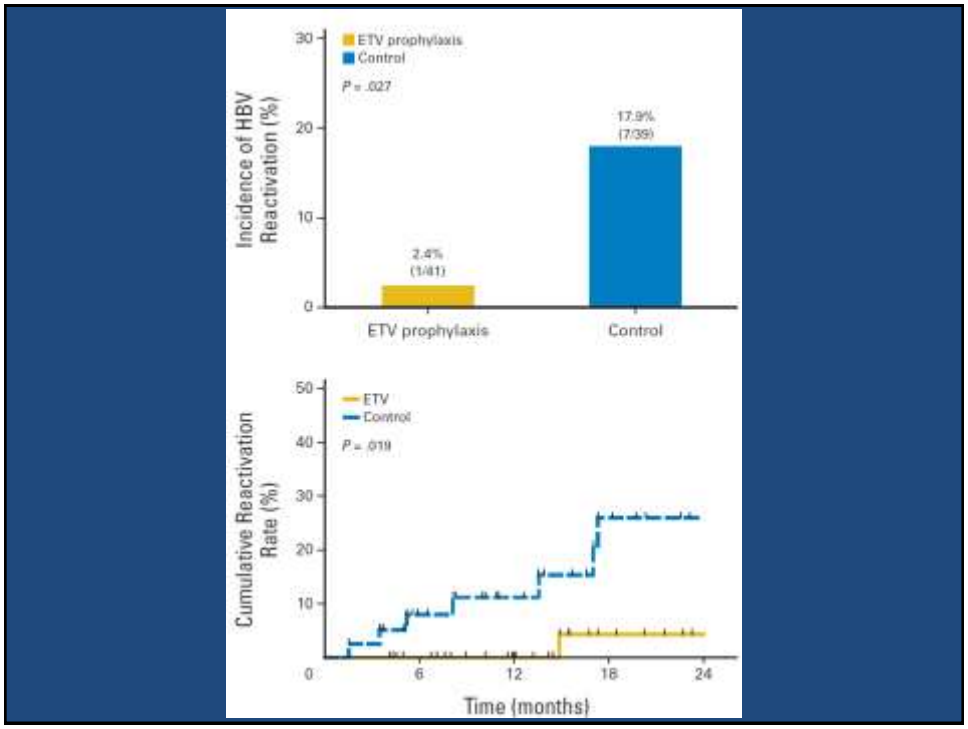
The high-risk group & OBI

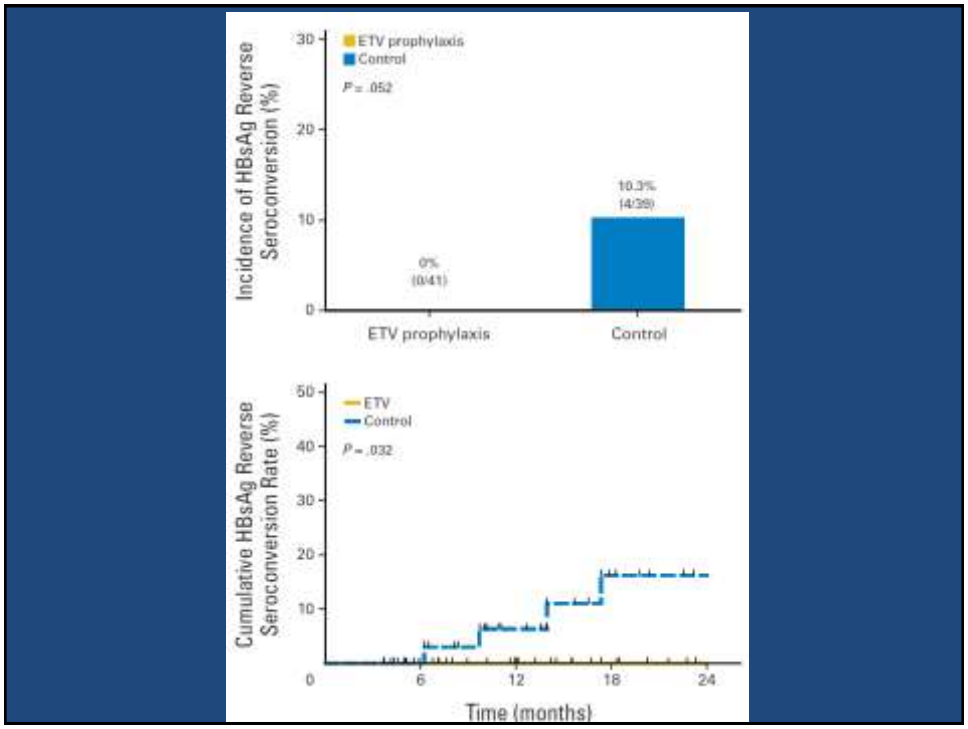
- B cell–depleting agents (rituximab, ofatumumab)

Randomized Controlled Trial of Entecavir Prophylaxis for Rituximab-Associated Hepatitis B Virus Reactivation in Patients With Lymphoma and Resolved Hepatitis B

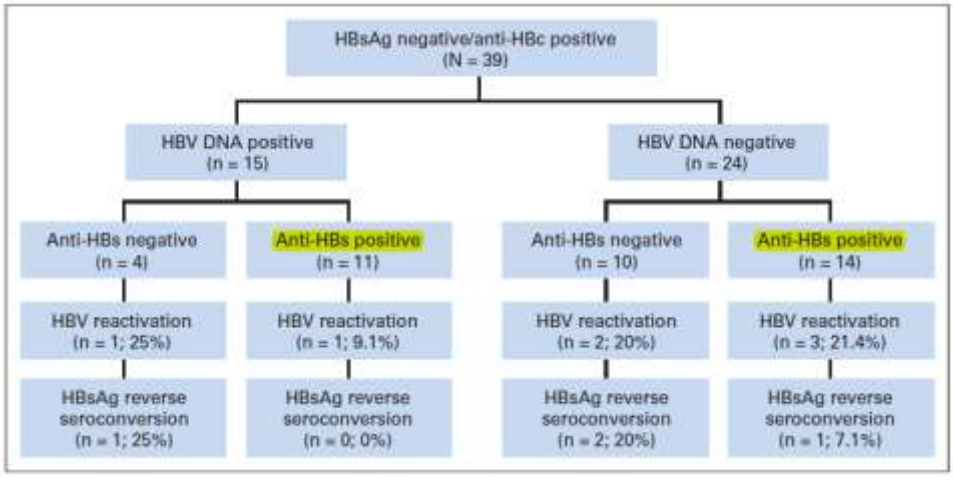
- 80 patients with lymphoma and resolved hepatitis B were randomly assigned to
  - Prophylactic entecavir (ETV) before chemotherapy to 3 months after completing chemotherapy (n 41)
  - Therapeutic ETV at the time of HBV reactivation and HBsAg reverse seroconversion since chemotherapy (n 39)

Yi-Hsiang Huang,et al. J Clin Oncol 31:2765-2772. 2013 by American Society of Clinical Oncology


Incidence of HBV Reactivation (%)
ETV prophylaxis
Control
P = .027
17.9% (7/39)
2.4% (1/41)
ETV prophylaxis
Control
Cumulative Reactivation Rate (%)
ETV
Control
P = .019
Time (months)


Incidence of HBsAg Reverse Seroconversion (%)
ETV prophylaxis
Control
P = .052
10.3% (4/39)
0% (0/41)
ETV prophylaxis
Control
Cumulative HBsAg Reverse Seroconversion Rate (%)
ETV
Control
P = .032
Time (months)

Randomized Controlled Trial of Entecavir Prophylaxis for Rituximab-Associated Hepatitis B Virus Reactivation in Patients With Lymphoma and Resolved Hepatitis B

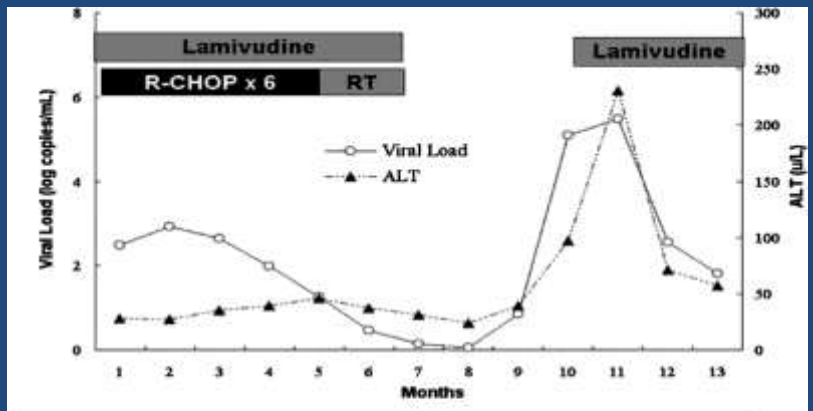


Yi-Hsiang Huang,et al. J Clin Oncol 31:2765-2772. 2013 by American Society of Clinical Oncology

The high-risk group & OBI

- The AGA *recommends* antiviral prophylaxis
  - at least 12 months after discontinuation of immunosuppressive therapy

Delayed HBV reactivation after premature cessation of preemptive lamivudine in a lymphoma patient receiving six courses rituximab (R) and CHOP



Month	1	2	3	4	5	6	7	8	9	10	11	12	13
ALC (cumm)	2184	1863	1912	2246	1371	1625	1344	1120	1040	956	1367	1455	1890
CD20 (%)	20	19	4.8	0.7	0	0	0	0	0	0	2	10	15
HBeAg	-									-			-
Anti-HBe Ab	+									+			+

Daniel Shouval, **Immunosuppression and HBV Reactivation** Semin Liver Dis 2013; 33(02):

The moderate-risk group & OBI

- The AGA *suggests* antiviral prophylaxis
  - –6 months after discontinuation of immunosuppressive therapy.

The moderate-risk group & OBI

- Patients treated with
  - TNF alpha inhibitors
    - (etanercept, adalimumab, certolizumab, infliximab)
  - other cytokine or integrin inhibitors
    - (abatacept, ustekinumab, natalizumab, vedolizumab
  - tyrosine kinase inhibitors
    - (imatinib, nilotinib)
  - dose >10mg prednisone daily for 4 weeks
  - anthracycline derivatives
    - (doxorubicin, epirubicin)

The low-risk group & OBI

- Patients treated with
  - AZA,6MP,MTX
  - intra-articular corticosteroids
  - any dose of oral corticosteroids daily for 1 week
  - <10 mg prednisone corticosteroids for 4 weeks

The low-risk group & OBI

- The AGA ***suggests against*** routinely using antiviral prophylaxis

K. Rajender Reddy et al. Gastroenterology 2015