



HEPATOCELLULAR CARCINOMA IN YOUNG PATIENTS WITH CHRONIC HBV INFECTION: CHALLENGES AND SOLUTIONS

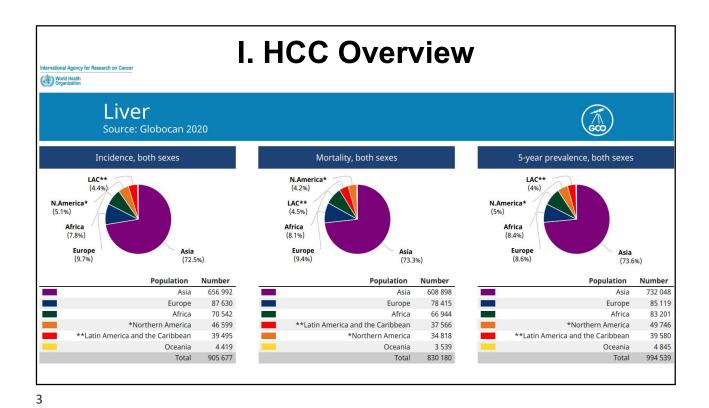


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CONTENT

- I. HCC Overview
- II. Clinical Cases
- III. Challenges of HCC management in young patients with chronic HBV infection
- IV. Solutions of HCC management in young patients with chronic HBV infection
- V. Conclusion





Global burden of primary liver cancer in 2020 and predictions to 2040 Global burden of primary liver cancer Liver cancer ranked among the top 3 causes of cancer death in 830,200 905,700 46 countries people were diagnosed people died from liver with liver cancer in 2020 cancer in 2020 The **number** of people **diagnosed** with or **dying** from liver cancer globally could increase by more than 55% between 2020 and 2040 if current rates do not change Liver cancer is a major cause of death in many countries. Efforts to reduce the incidence of preventable liver cancer should be prioritised to avoid the predicted rise in people diagnosed with liver cancer. Harriet Rumgay et al. Journal of Hepatology 2022 vol. 77 j 1598–1606

Estimated number of new cases of liver cancer in Asia from 2020 to 2040, Incidence, both sexes, age [0–85+], based on CANCERTOMORROW | IARC

Population	Annual Population		Number of New Cases		Change in Number of Case
	2020	2040	2020	2040	
Kazakhstan	18,776,707	22,370,403	1039	1707	+64.3%
Kuwait	4,270,563	5,152,526	128	482	+276.6%
Kyrgyzstan	6,524,191	8,307,138	476	911	+91.4%
Lao People Democratic Republic	7,275,556	8,971,941	1272	2453	+92.8%
Lebanon	6,825,442	6,376,397	172	302	+75.6%
Malaysia	32,365,998	38,754,576	2149	3906	+81.8%
Maldives	540,542	556,282	29	83	+186.2%
Mongolia	3,278,292	4,089,199	2236	4506	+101.5%
Myanmar	54,409,794	61,201,610	5466	8529	+56.0%
Nepal	29,136,808	34,889,298	524	1007	+92.2%
Oman	5,106,622	64,37,413	128	364	+184.4%
Pakistan	220,892,331	302,129,186	5331	9901	+85.7%
Palestine	5,101,416	7,599,231	164	407	+148.2%
Philippines	109,581,085	135,618,864	10,594	19,882	+87.7%
Qatar	2,881,060	3,628,689	56	256	+357.1%
Republic of Korea	51,269,183	49,783,741	14,788	23,763	+60.7%
Saudi Arabia	34.813.867	42,473,029	1145	3542	+209.3%
Singapore	5,850,343	6,445,489	1347	3213	+138.5%
Sri Lanka	21,413,250	22,186,243	354	540	+52.5%
Syrian Arab Republic	17,500,657	30,153,278	376	1093	+190.7%
Tajikistan	9,537,642	13,845,878	304	676	+122.4%
Thailand	69,799,978	69,008,295	27,394	42,614	+55.6%
Timor-Leste	1,318,442	1,809,281	48	83	+72.9%
Turkey	84,339,067	94,131,585	5649	10,733	+90.0%
Turkmenistan	6,031,187	7,408,523	317	554	+74.8%
United Arab Emirates	9,890,400	10,648,314	83	452	+444.6%
Uzhokietan	33,469,199	40,608,381	1629	3223	±97 9%
Viet Nam	97,338,583	107,795,035	26,418	41,124	+55.7%
Yemen	29,825,968	42,670,023	745	1541	+106.8%
Totals	4,616,030,644	5,164,031,646	643,637	970,231	+50.7%

Cancers 2022, 14, 4473. https://doi.org/10.3390/cancers14184473. Published: 15 September 2022

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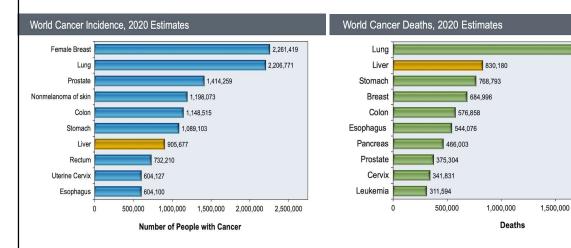
Late Detection of HCC. It is very serious!

2020 Global Cancer Incidence Estimates

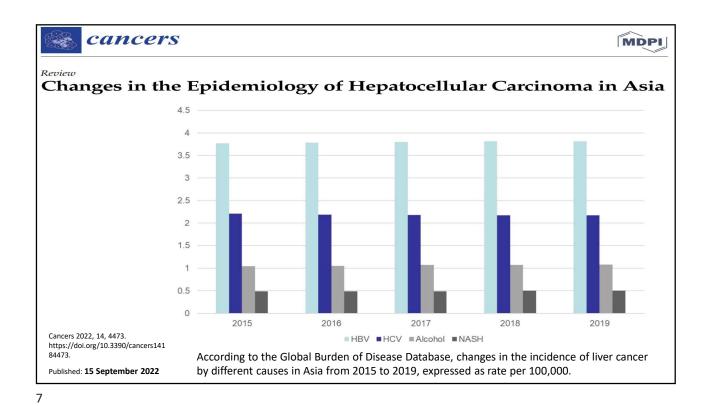
2020 Global Cancer Death Estimates

1,796,144

2,000,000



Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021 Feb 4.



HBV IS THE MAJOR CAUSE OF HCC IN VIET NAM 2.7% 9% 26% 62.3% 81.3% 81.3% HBV/HCV HBV/NHCV NRBV/NHCV

Northern Vietnam, from 2010 to 2017.

Data from 198 advanced HCC patients.

1, Nguyen-Dinh SH et al . World J Hepatol 2018 January 27; 10(1): 116-123.

2, Le et al. Cancer Control Volume 26: 1-6. 2019.

Southern and Central Vietnam, from

Data from 24091 HCC patients.

2010 to 2016.

Case 1: A 9-year-old boy with HCC

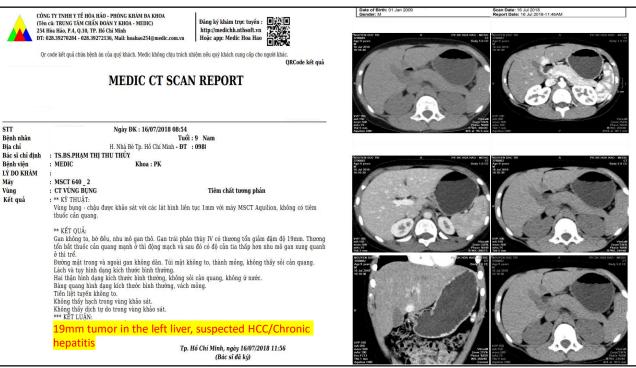
- A 9-year-old boy, lived in Binh Chanh- HCM City
- 42 kg, no specific symptoms
- Family history: both parents and older brother had HBV infection
- The father went for his HBV check-up. His doctor advised him to do HBV screening for his children.
- They visited doctors only twice before without any treatment, no follow up.
- The boy were taken to Medic Medical Center in July 2018.

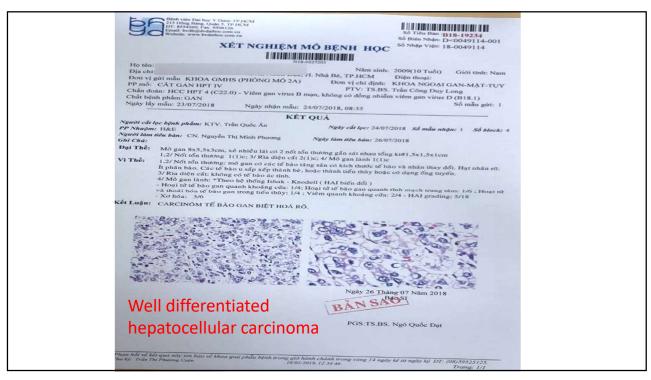
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Case 1: A 9-year-old boy with HCC

- CBC: normal
- Bilirubin-T: 0.36 mg/dL
- AST: 37 U/L ALT: 36 U/L GGT: 22 U/L
- Creatinin: 0.57mg/dL
- HBsAg: positive, HBeAg: negative, AntiHCV: negative
- HBV DNA: 4311 copies/mL
- AFP: 1590 ng/mL
- AFP-L3: <0.5%
- PIVKA II: 15 mAU/mL
- CEA: 0.7 ng/mL CA19-9: 7.4 U/ml







Case 1: A-9 year-old boy with HCC- After 2 years

• CBC: normal

• Bilirubin-T: 0.59 mg/dL

• AST: 26 U/L ALT: 27 U/L GGT: 23 U/L

Creatinin: 0.57mg/dL

• HBsAg: positive, HBeAg: negative, AntiHCV: negative

• HBV DNA: not detected

AFP: 2 ng/mL

AFP-L3: <0.5%

PIVKA II: 12 mAU/mL

• CEA: 0.1 ng/mL CA19-9: 8.3 U/ml

Ultrasound: Nothing abnormal detected

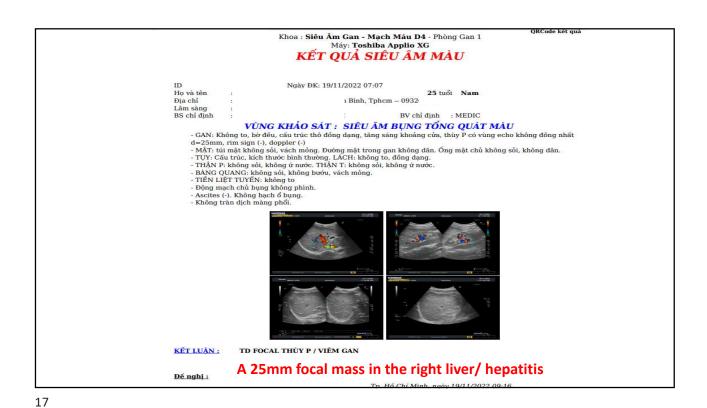
Case 2: A 25-year- old young man with HCC

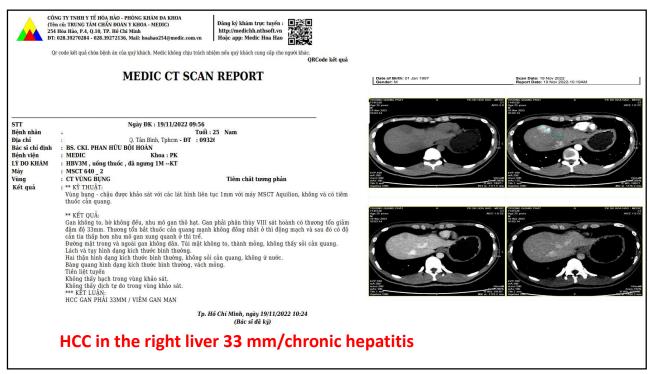
- A 25- year- old young man, single
- W: 62kg, H: 178cm- No specific symptoms.
- Occupation: Worker in Ho Chi Minh City
- No alcohol, no smoking
- No operation, no blood transfusion
- Family history: Mother and older brother had HBV infection
- Did company annual health check, was aware of having chronic HBV infection, no doctor visit, used traditional medicine for 2 months
- Felt fatigue, had an upset stomach, went to Medic medical center in November 2022

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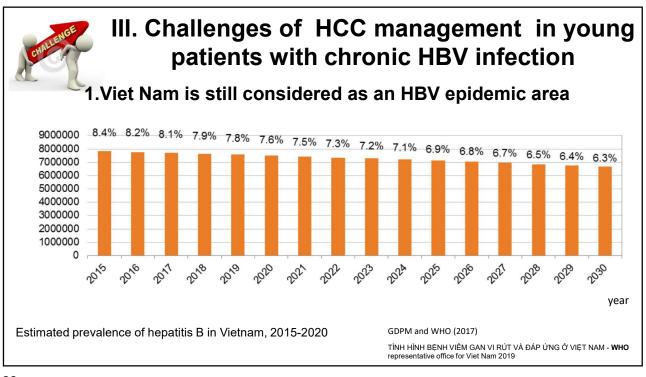
Case 2: A 25-year-old young man with HCC

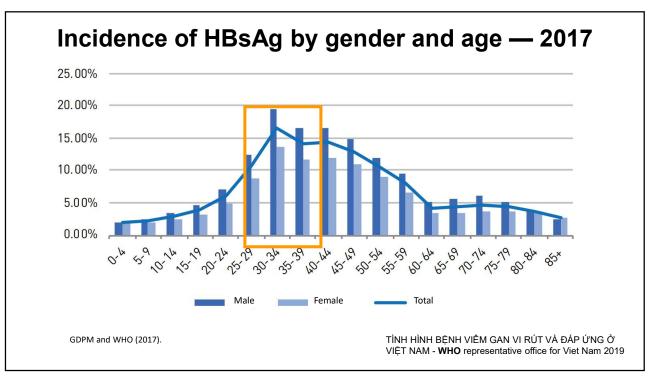
- CBC: normal
- Bilirubin-T: 0.76 mg/dL
- AST: 32 U/L
 ALT: 80 U/L
 GGT: 35 U/L
- Creatinin: 0.9mg/dL
 – eGFR: 118
- HBsAg: positive, HBeAg: positive, AntiHBc IgM: negative
- AntiHCV: negative
- HBV DNA: 49781 copies/mL
- AFP: 1131 ng/mL
- CEA: 0.9 ng/mL CA19-9: 12 U/ml









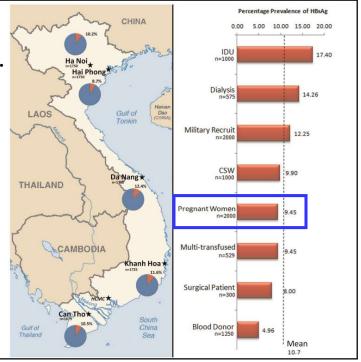


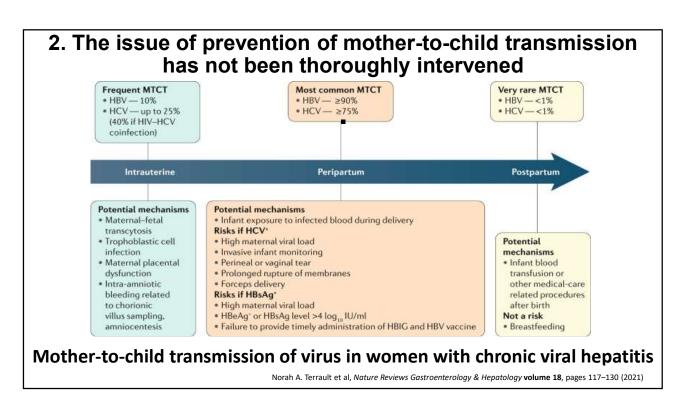
Map of Viet Nam Depicting the Prevalence of HBsAg in 5 Regions.

The map depicts the percentage HBsAg positives in Ha Noi, Hai Phong, Da Nang, Khanh Hoa and Can Tho. To the right is a graph depicting the prevalence of HBsAg in each of the study groups in the 5 study sites in Viet Nam.

$$n = 8654$$

Linda Dunford et al. A Multicentre Molecular Analysis of Hepatitis B and Blood-Borne Virus Coinfections in Viet Nam . PLoS ONE | www.plosone.org June 2012 | Volume 7 | Issue 6 | e39027





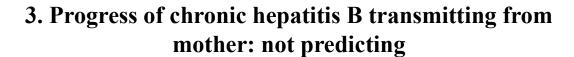
Hepatitis B in pregnancy

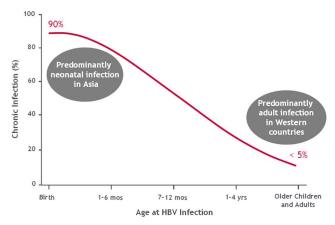
PERINATAL HBV TRANSMISSION

Perinatal transmission is a common mode of HBV transmission worldwide^[1]. HBV infection in newborns is defined as hepatitis B surface antigen (HBsAg) positivity 6 mo after birth. Antibody to hepatitis B e antigen (anti-HBe) and anti-hepatitis B core antigen cross the placental barrier and disappear in nearly all babies before 12 and 24 mo of age, respectively^[8]. Therefore, they simply represent the transplacental maternal antibodies and are not indicators of HBV infection status^[8].

Without prophylaxis the risk of mother-to-child transmission is very high. It varies with the HBeAg/anti-HBe status of mothers, being 70%-90% for HBeAg-positive mothers, 25% for HBeAg-negative/HBeAb-negative mothers and 12% for HBeAg-negative/anti-HBe-positive mothers [9-12]. Maternal screening programs aimed at identifying HBsAg-positive mothers are part of pregnancy routine examinations in most countries. Once HBsAg-positive mothers are identified, their babies receive passive-active immunoprophylaxis at birth to reduce vertical HBV transmission [3]. Passive immunoprophylaxis consists of the administration of hepatitis B immune globulin (HBIG) whereas active immunoprophylaxis is the administration of hepatitis B vaccine [1,3].

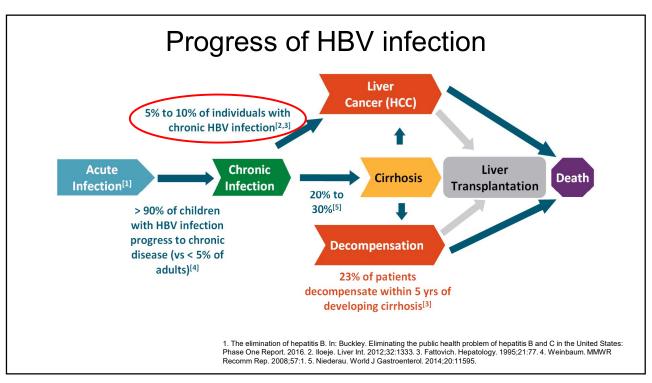
Guglielmo Borgia et al. World J Gastroenterol 2012 September 14; 18(34): 4677-4683



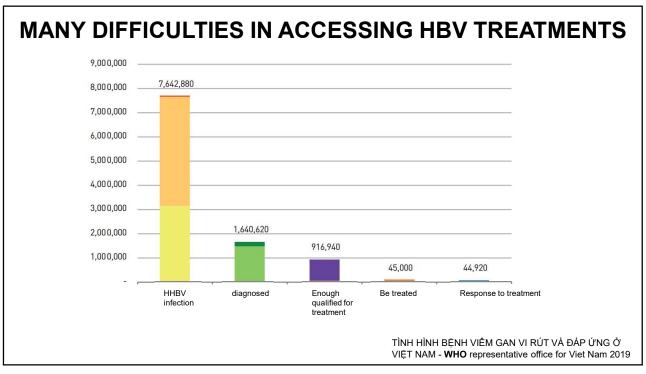


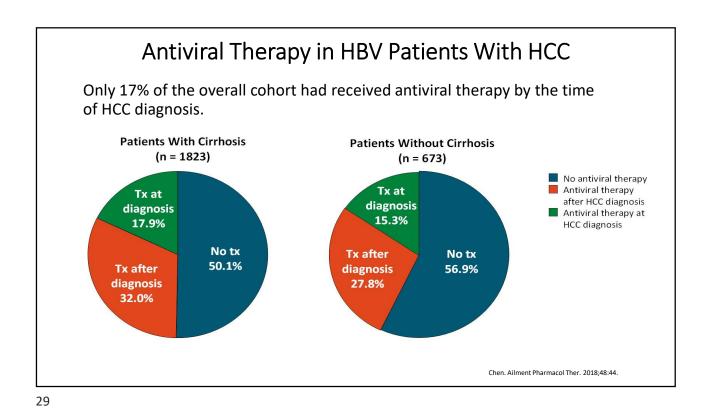
Progression to Chronic Infection is Dependent on the Age at Acute HBV Infection

Asian Liver Center. 2007 Physician's Guide to Hepatitis B: A Silent Killer. http://liver.stanford.edu/files/2007Handbook.pdf. Accessed November 7, 2007.

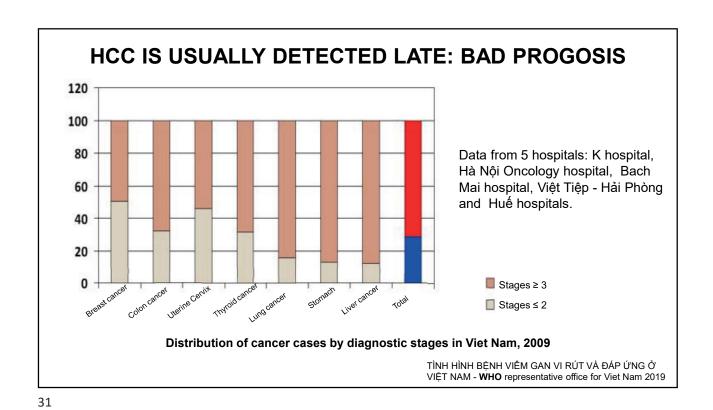








5. Clinical manifestation of HBV, HCC



6. Knowledges, experiences of healthcare staff: CME





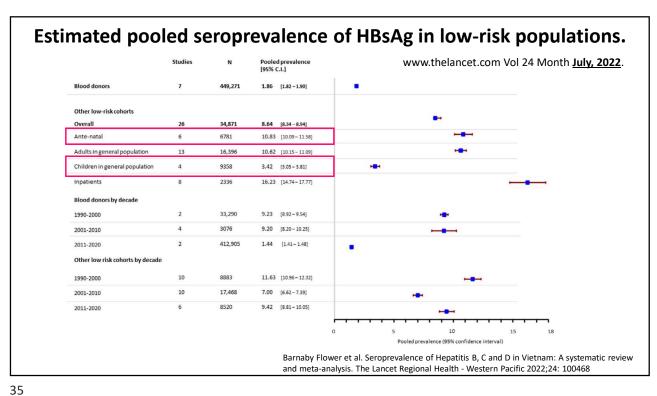
IV. Solutions of HCC management in young patients with chronic HBV infection

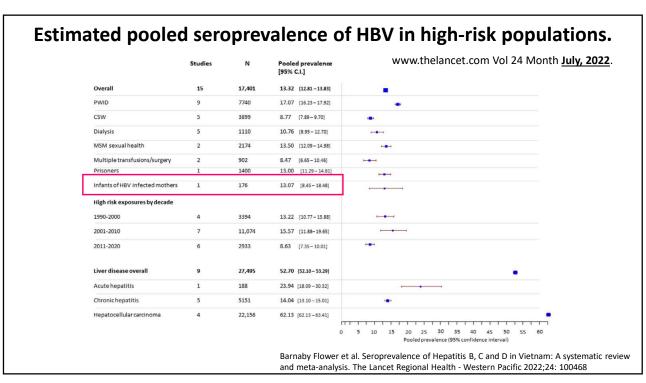
1. HBV Screening, especially in high risk group

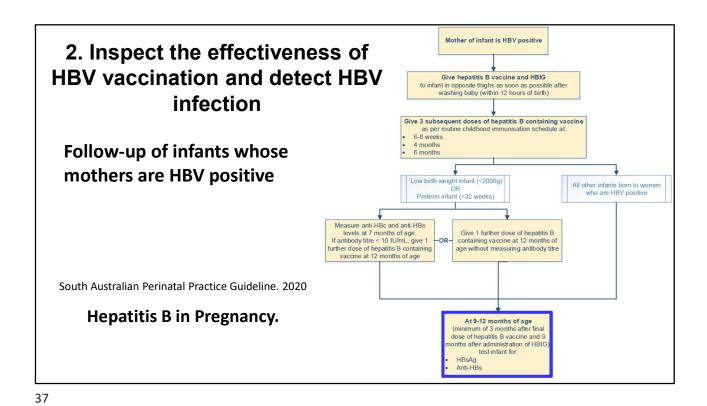
Perinatal transmission is a common mode of HBV transmission in Vietnam. Without prophylaxis is the risk of mother-to-child transmission is very high

Gần như tất cả các trường hợp mắc viêm gan B mạn tính ở Việt Nam là do lây truyền từ mẹ sang con (truyền dọc) hoặc bị lây nhiễm khi còn nhỏ (truyền ngang). Gánh nặng bệnh tật và phương thức lây truyền chỉ ra rằng truyền dọc chiếm khoảng 57% các ca nhiễm, và lây truyền ngang chiếm 43%. Tỷ suất lây truyền dọc dự kiến sẽ tăng lên khi miễn dịch do vắc xin được cải thiện và làm giảm tỷ suất lây truyền nagng. Hiện tượng mắc viêm gan B ở trẻ sau 5 tuổi sẽ vẫn xảy ra, nhưng phản ứng miễn dịch trưởng thành có nghĩa là nhiễm trùng cấp tính ở tuổi thiếu niên và trưởng thành hầu như luôn luôn (95% trường hợp) liên quan đến tự khỏi.

TÌNH HÌNH BỆNH VIÊM GAN VI RÚT VÀ ĐÁP ỨNG Ở VIỆT NAM - WHO representative office for Viet Nam 2019







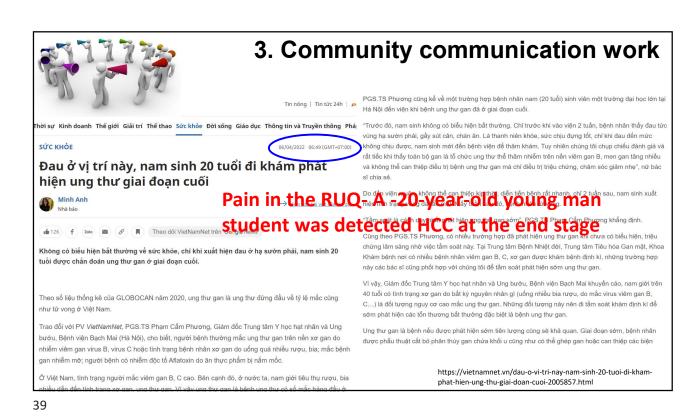


- 1. Indicators for the testing of mothers. These include the proportion of mothers tested for HBsAg, the proportion of mothers testing positive for HBsAg and the proportion of HBsAg-positive mothers tested for HBV DNA or HBeAg.
- **2. Indicators for the management of mothers.** These include the proportion of HBsAg-positive mothers eligible for prophylaxis and the proportion of eligible women who receive antivirals.
- **3. Indicators for the management of infants.** These include the proportion of exposed infants receiving a timely birth dose, the proportion of exposed infants receiving HBIG, the proportion of all infants receiving a timely birth dose and the proportion of exposed infants tested for infection at 7–12 months of age.

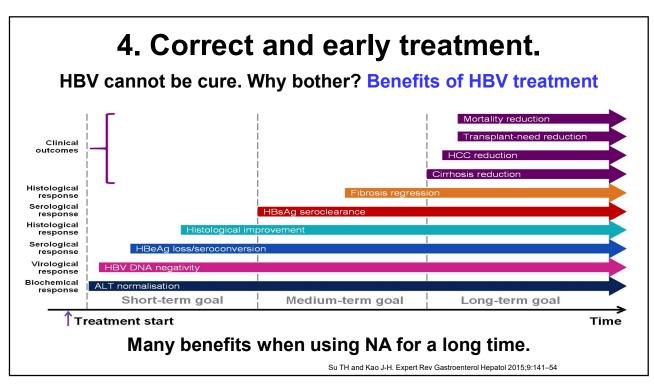
Outcome indicator

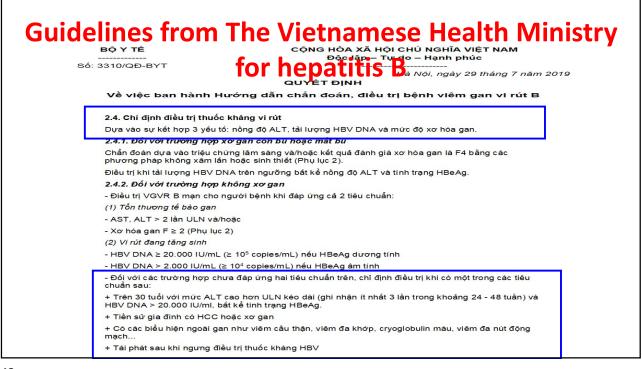
The rate of mother-to-child transmission is the incidence of HBV infection in infants born to HBsAg-positive mothers. It is calculated by dividing the number of HBsAg-positive infants at post vaccination serological testing by the number of infants tested at 7–12 months of age (1–2 months after completion of the last dose of vaccine according to the WHO position paper on immunization). The data source is the follow up of infants born to HBsAg-positive mothers (55).

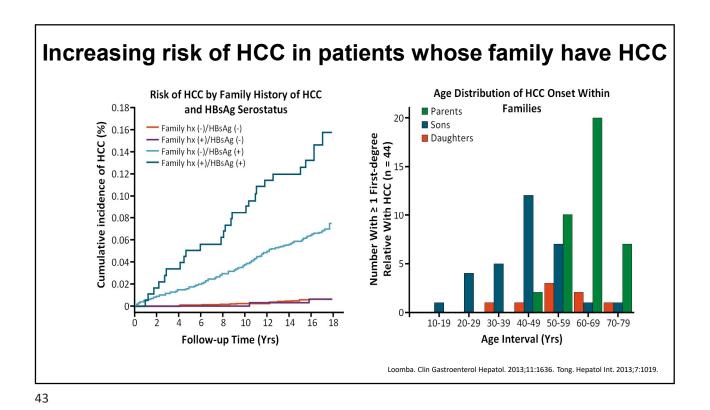
PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HEPATITIS B VIRUS: GUIDELINES ON ANTIVIRAL PROPHYLAXIS IN PREGNANCY. WHO JULY 2020.





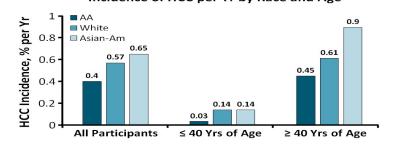




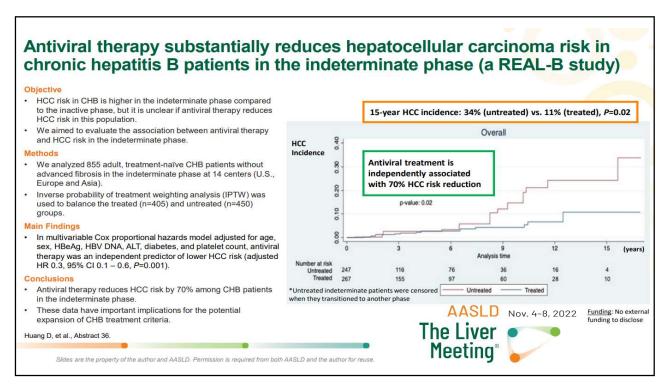


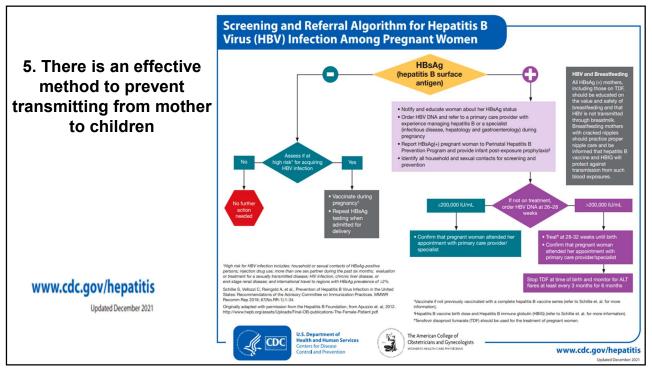
Risk of HCC by different ages and races

- VA study of 8320 patients with chronic hepatitis B; 39% African-American, 95% male, followed for 7.1 yrs
 - Risk of HCC is highest among Asian-Americans, followed by Whites and African-Americans
 Incidence of HCC per Yr by Race and Age



Mittal. Clin Gastroenterol Hepatol. 2018;16:252.





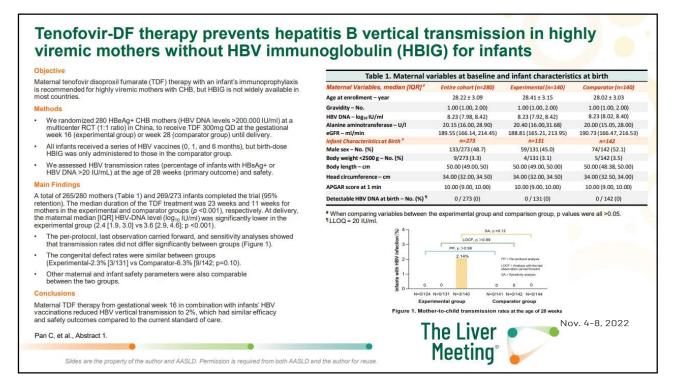
Guidelines from The Vietnamese Health Ministry for pregnant women with HBV

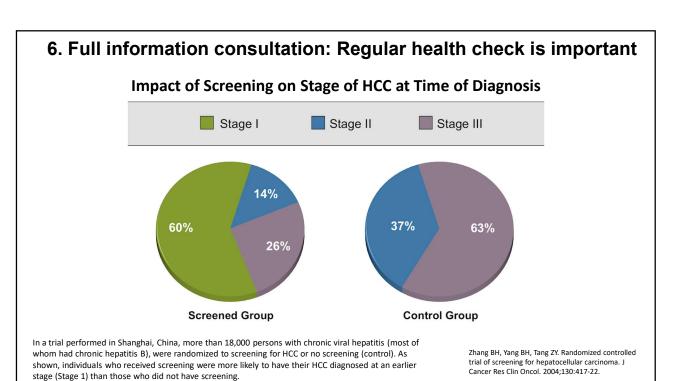
QUYẾT ĐỊNH VỀ VIỆC BAN HÀNH HƯỚNG DA GA CỊCHO ĐỀU TRỊ BỆNH VIỆM GAN VI RÚT B

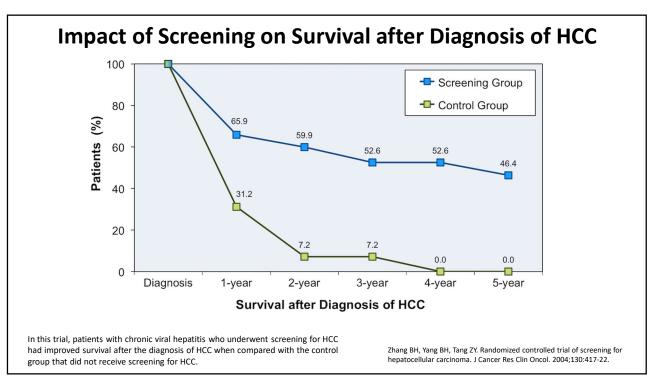
2.7.4. Phụ nữ mang thai

- Đối với phụ nữ mang thai có HBsAg dương tính và chưa điều trị kháng vi rút, cần đánh giá các tiêu chuẩn điều trị
- + Nếu đủ tiêu chuẩn: điều trị bằng TDF
- + Nếu không đủ tiêu chuẩn: Theo dối và điều trị dự phòng lây nhiễm HBV từ mẹ sang con (mục 2, phần IV)
- Đối với phụ nữ đang điều trị viêm gan B mạn muốn có thai, nếu đang điều trị bằng thuốc không phải
 TDF thì chuyển sang TDF trước khi dự kiến có thai ít nhất 2 tháng.
- Đối với phụ nữ mới phát hiện có thai trong khi đang điều trị kháng vi rút, tiếp tục điều trị TDF, nếu đang điều trị thuốc không phải TDF thì chuyển sang TDF.

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Hepatocellular carcinoma in children and young patients with chronic HBV infection and the usefulness of alpha-fetoprotein assessment

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Cevwords

alpha-fetoprotein, HBeAg seroconversion, hepatocellular carcinoma, interferon, liver cirrhosis

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Cancer Medicine 2016; 5(11):3102-3110

doi: 10.1002/cam4.917

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Abstract

since childhood

The aims of the study were to elucidate the clinical characteristics of patients who developed hepatocellular carcinoma (HCC) related to persistent HBV infection since childhood and to investigate usefulness of assessing alpha-fetoprotein (AFP) in this population. A nationwide multicenter survey of children with chronic HBV infection was performed. Among 548 patients, 15 patients developed HCC at the median age of 15 years (range 9-36), including 13 males and 2 females. A case-control comparison showed that HBeAg seroconversion and liver cirrhosis were associated with the occurrence of HCC. Of the 15 HCC patients, 5 were treated with interferon and none of them responded to interferon therapy as compared with 12 of the 17 responders in the control group. Of the 15 patients, 10 died and 9 of the 10 who died never visited any medical facilities until diagnosis of HCC, while the remaining 5 surviving patients never stopped their clinic visits. The usefulness of AFP assessment was shown by the findings that AFP levels were elevated in all HCC cases, that elevations in AFP levels were detected prior to the diagnosis in the surviving patients, and that sensitivity of AFP as a diagnostic test for HCC was very high among 40 patients including our 14 and an additional 26 collected from the literature. HBeAg seroconversion and liver cirrhosis are associated with the occurrence of HCC. Regular measurement of AFP might be helpful to watch for the occurrence of

HCC when following children and young patients with chronic HBV infection

7. Key: HBV vaccination



Hepatitis B vaccination has been administered in the high risk regions of our country since 1997

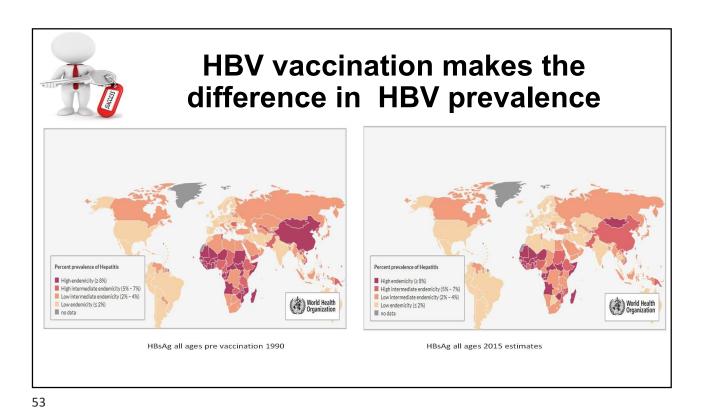


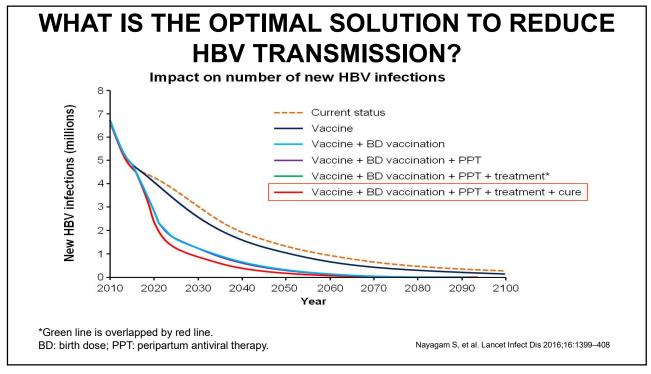
http://eva.vn/lam-me/nhung-chang-duong-cua-chuong-trinh-tiem-chung-mo-rong-tai-vn-c10a245133.html



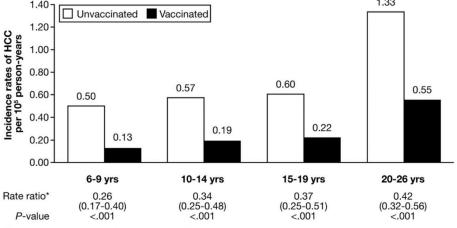
Năm 2003, văc xin phòng bệnh viêm gan B được triển khai đồng loạt tại tắt cả các tuyên

2003





Comparison of HCC incidence rate ratios (95% CI) by age group cohorts born before and after the commencement of the universal hepatitis B vaccination program in Taiwan 1.40 Univaccinated Vaccinated



*Rate ratio of vaccinated/unvaccinated birth cohort

Chang et al. Gastroenterology, Vol 151 (3), Long-term Effects of Hepatitis B Immunization of Infants in Preventing Liver Cancer, Pages 472–480.e1, 2016

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Take antiviral drugs





Ingest phytochemicals in vegetables and fruits



Quit smoking

文

Keep regular aerobic exercise and lose weight





Quit drinking

Cancers 2022, 14, 4473. https://doi.org/10.3390/cancers14184473. Published: **15 September 2022**



V. CONCLUSION

- Screening to detect HBV in all patients who have high risk or perform general check
- Should not be cavalier about HBV in any age group. It is always necessary to periodically screen for HCC to detect HCC as early as possible so that the treatment is more effective and the prognosis is better.
- Important information: Chronic hepatis B usually has no symptom, even with cirrhosis and HCC
- All pregnant women have to check for HBV infection to have suitable handling, either consultant or treatment to prevent transmission to child.
- Important: Full consultant; on time diagnosis; correct treatment
- HBV vaccination makes a difference in the fight against HBV infection.

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