

Profile of Liver Function Tests, Serology and Demographic Status of Children with Hepatitis B and Comorbidities at RSUD Dr. Soetomo in 2019 - May 2023

Kainat Rahman^a, Aryati^{a,b}, Ulfa Kholili^{a,c}, Bagus Setyoedi^{a,d}

^aemail: kainat.rahman-2017@fk.unair.ac.id

^aFaculty of Medicine, Airlangga University, Jl. Mayjen Prof. Dr. Moestopo No.47 Surabaya 60131, Indonesia

^bDepartment of clinical pathology, Dr. Soetomo General Academic Hospital, Jl. Mayjen Prof. Dr. Moestopo No.6-8 Surabaya 60286, Indonesia ^cDepartment of internal medicine, Dr. Soetomo General Academic Hospital, Jl. Mayjen Prof. Dr. Moestopo No.6-8 Surabaya 60286, Indonesia, ^dDepartment of paediatrics, Dr. Soetomo General Academic Hospital, Jl. Mayjen Prof. Dr. Moestopo No.6-8 Surabaya 60286, Indonesia

Abstract

Viral hepatitis is a global health problem. The risk of hepatitis B infection increases due to 95% transmission during pregnancy and 5% intra-uterine period. Infection in early life has a 90% risk of becoming chronic liver disease. There have not been many studies that suggest the profile of liver function test, serology and demographic status of children with hepatitis B diagnosis. This study aims to determine the profile of liver function test, serology and demographic status of children patients at RSUD Dr Soetomo Surabaya diagnosed with hepatitis B and comorbidities. This study used an operational descriptive method and total sampling technique of 21 child patients, 14 males (66.66%), 7 females (33.33%) and an average age of 9.7 years (9 months-17 years). Normality test results showed normal distribution of albumin ($p=0.832$), and abnormal bilirubin ($p=0.004$), total bilirubin ($p=0.004$), SGOT ($p=0.000$) and SGPT ($p=0.000$). Mean albumin was 3.58 g/dL (2.06-4.91), median SGOT 86 u/L (2-832), median SGPT 56 u/L (18-356), median total bilirubin 2.56 mg/dL (0.45-12.67) and median recruited bilirubin 1.54 mg/dL (0.10-9.94). SGOT and SGPT were found to be increased in 17 patients (80.95%) and 12 patients (57.14%) and albumin was found to be decreased in 7 patients (33.33%). Increased SGPT in 2 patients without comorbidities and 10 patients with comorbidities. decreased albumin was not found in pediatric patients without comorbidities and in pediatric patients with comorbidities found decreased albumin levels and increased levels of direct bilirubin and total bilirubin influenced by comorbidities at Dr. Soetomo Surabaya Hospital.

Keywords: Hepatitis B; SGOT; SGP; Albumin; children with hepatitis B

1. Introduction

Viral hepatitis causes health problems globally. WHO estimates by 2019 that 296 million individuals will be living with chronic hepatitis B infection with 1.5 million new infections each year, leading to 820,000 deaths, mostly due to cirrhosis and hepatocellular carcinoma (WHO, 2022). 75% of the global population affected by HBV is from Southeast Asia and the Western Pacific (Zhang et al., 2019). Globally, hepatitis B cases are highest in Southeast Asia and Sub-Saharan Africa, and lowest in high-income countries (Schollmeier et al., 2023). It is predicted that each year there are up to 2 million new infections in children younger than 5 years of age. Most infected children are infected during the birth

period through vertical transmission or during childhood through horizontal transmission (Stinco et al., 2021). There is a lack of information on HBV prevalence in Indonesia due to an insufficient disease surveillance system, unreporting of acute and chronic infections, geographical barriers when collecting data on 250 million people across more than 17,000 islands; limited HBV testing facilities lead to many undiagnosed individuals (Dakl & Alnuaimy, 2020).

The first rate of chronic infection is highly variable from > 6 per cent in Africa and the Western Pacific islands to < 1 per cent in the United States. With a large number of chronic infected individuals, the infection spreads easily from parent to child, playmates or exposure to blood or body fluids from infected individuals (Scheifele, 2019). Among infected individuals, 15% to 40% are at risk of developing liver cirrhosis, liver failure and hepatocellular carcinoma (Pronocitro et al., 2017).

Indonesia is one of the country most often exposed to hepatitis B. Transmission of hepatitis B usually occurs vertically, from mother to child. The risk of developing chronic hepatitis B increases as 95% of transmission occurs during pregnancy, while 5% is during the intrauterine period (Lestari et al., 2023). HBV infection in early life has a 90% risk of becoming chronic hepatitis B compared to infection in adulthood. Chronic infection in young adults is only 1% to 2%. This is an increase from the prevalence in 2007. The most common infection was HBV at 21.8% (Rasmiatin et al., 2023).

HBsAg and Anti-HBs are viral surface antigens derived from envelope proteins. HBsAg positive is a characteristic of hepatitis B virus infection, which is detected 1-10 weeks after exposure or 1-6 weeks before symptoms appear as well as elevated alanine aminotransferase (ALT). Infant HBV infection is through mother-to-child transmission, with an HBsAg-seropositive rate in pregnant women of 12.5%. Mothers with high DNA load and Hepatitis B e Antigen (HBeAg) positivity are at risk of HBV-positive infants (Peng et al., 2019).

The Advisory Committee on Immunisation Practices (ACIP) recommends hepatitis B surface antigen (HBsAg) testing for all pregnant women and testing HBsAg-positive pregnant women with hepatitis B virus deoxyribonucleic acid (Schillie et al., 2018). The prevalence of concurrent HBsAg and anti-HBs is low at 1.2%, with some anti-HBs disappearing after the treatment period. The co-existence of HBsAg and anti-HBs, do not identify a specific phenotype of chronic hepatitis B, and do not affect clinical outcomes (Lee et al., 2020).

Given the high prevalence of chronic HBV in mothers, HBV vaccination of newborns within the first 24 hours after birth should be included in current immunisation schedules, and the use of TDF-based ART regimens in combination with lamivudine or emtricitabine is recommended during pregnancy (Yendewa et al., 2021). In 1849 children tested, 25 were HBsAg positive with a HBsAg positive rate of 1.35%, 92% or 23 children were born to HBeAg positive mothers (Jiang et al., 2021).

There have been not many studies that propose the Profile of liver function test, serology and demographic status of children diagnosed with hepatitis B at RSUD Dr. Soetomo so that this research will help the hospital in obtaining these data based on the above problems, the researcher is interested in knowing the Profile of liver function test, serology and demographic status of children at RSUD Dr. Soetomo Surabaya diagnosed with hepatitis B and comorbidities.

2. Method

This study used a descriptive observational research design with secondary data in the form of medical records of hepatitis B children with accompanying diseases aged <17 years of inpatient and

outpatient care at RSUD Dr Soetomo from 2019 to May 2023.

There were 21 children diagnosed with hepatitis B and its associated comorbidities. Data on patient characteristics were collected, such as gender and age. The age category was divided into 3 groups, which were 1 month -1 year old, 2-10 years old, 11-17 years old. The results of liver function test, serology and patient outcomes were collected.

3. Result

Tabel 1 Demographics of Children's Patients by Age

Age Category	Frequency (n)	Presentage (%)	Min	Max	Mean (Std.def)
1 month - 1 year	1	4.8			
2-10 years	9	42.9	0.75	17	9.70 (5.69)
11-17 years	11	52.4			
Total	21	100			

Table 1 describes the number of samples by age. Categorized as under 1 year with a percentage of 4.8%, 2-10 years with a percentage of 42.9% and 11-17 years 52.4%. The mean age of children with hepatitis B and its accompanying diseases was 9.7 years with the youngest age at 9 months and the oldest age at 17 years.

Tabel 2 Demographics of Children's Patients by gender

Jenis Kelamin	Frekuensi	Presentase (%)
Perempuan	7	33,33
Laki laki	14	66,66
Total	21	100

Table 2 shows the number of samples based on gender. The demographic of male patients is 14 patients, which is 66.66% and female is 33.33%.

Table 3 Liver function test results of Albumin, Direk bilirubin, total bilirubin, SGOT and SGPT

Liver function	N	Normal	Not Normal
		Mean (Std.def)	Median (Min- Max)
Albumin (g/dL)	17	3.58 (0.15)	
Bilirubin Total (mg/dL)	12		2.56 (0.45-12.67)
Bilirubin Direk (mg/dL)	12		1.54 (0.10-9.94)
SGOT (U/L)	21		86 (2-832)
SGPT (U/L)	21		56 (18-356)

Table 3 indicates the results of the normality test of normal data distribution of albumin ($p=0.832$) and abnormal data distribution of bilirubin rec ($p=0.004$), total bilirubin ($p=0.004$), SGOT ($p=0.000$) and SGPT ($p=0.000$). Mean albumin found 3.58 g/dL (2.06-4.91), median SGOT found 86 u/L (2-832), median SGPT found 56 u/L (18-356), median total bilirubin found 2.56 mg/dL (0.45-12.67) and median recruited bilirubin found 1.54 mg/dL (0.10-9.94). In the SGOT examination, there was an increase in 17 patients (80.95%), and SGPT in 12 patients (57.14%), albumin examination was found to be decreased in 7 patients (33.33%). In the GGT liver function test, there were 2 data (9.52%) out of 21 data. In the serological examination of HBeAg and Anti-HBs each found 1 data (4.76%) of 21 total data.

Table 4 Overview of the Comorbid Diseases in Paediatric Patients

Hepatitis B			n
Without Comorbidities			3
With Comorbidities			18
- Acute encephalitis	- Laryngeal stenosis	- Arterial embolism and thrombosis	
- Jaundice	- Pericardial effusion	- Plasma protein metabolism disorders (4)	
- Conjunctivitis	- Chronic renal failure	- Liver cell carcinoma (2)	
- Hypothyroidism	- White blood cell disorders	- Neoplastic anaemia (2)	
- Septic shock (2)	- Septicaemia	- Ventricular septal defect	
- Optic neuritis	- Hypokalaemia (2)	- Malignant neoplasm of the retina	
- Pneumothorax	- Down's syndrome	- Calcium metabolism disorders	
- Ascites	- Hemorrhagic fever	- Acute lymphoblastic leukaemia (2)	
- Lymphangioma	- Congenital hypothyroidism	- Intracranial and granulomas	
- Anaemia (2)	- Bile duct obstruction	- Craniopharyngeal tract neoplasms	
- Tuberculosis	- Diabetes insipidus	- Lepromatous leprosy	
- Hydrocephalus	- Malignant neoplasm	- Iron deficiency anaemia	
- Abscess	- Erythema nodosum	- Keratoconjunctivitis	
- Hepatitis A	- Acute periodontitis	- Atrial septal defect	
- Liver abscess	- Joint contractures	- Congenital laryngomalacia	
- HIV	- Respiratory failure	- Adrenocortical insufficiency	
- Malnutrition (4)	- Thrombocytopenia	- Gastroenteritis and colitis (2)	
- Endometriosis	- Acute renal failure	- Acute upper respiratory tract infection (2)	
- Rubella	- Pneumonia	- Craniosynostosis	
Total			21

Table 4 shows a picture of hepatitis B patients who did not have comorbidities as many as 3 patients (14.28%), and who had comorbidities along with hepatitis B as many as 18 patients (85.71%).

Table 5 Overview of SGPT Tests

SGPT	N
SGPT Normal (<50 u/L)	9
<ul style="list-style-type: none"> - Without comorbidities - Jaundice - Septic shock - Ascites - Septicaemia - Hypokalaemia - Hydrocephalus 	<ul style="list-style-type: none"> - Down syndrome - Joint contractures - Bleeding fever - Thrombocytopenia - Respiratory failure - Malnutrition (3) - Acute renal failure - Liver cell carcinoma
<ul style="list-style-type: none"> - Arterial embolism and thrombosis - Acute lymphoblastic leukaemia (2) - Acute upper respiratory tract infection - Plasma protein metabolism disorders (2) - Neoplastic anaemia (2) - Ventricular septal defect - Tuberculosis 	
SGPT High (>50 u/L)	12
<ul style="list-style-type: none"> - Without comorbidities (2) - Acute encephalitis - Conjunctivitis - Pneumonia - Endometriosis - Anaemia (2) - Septic shock - Malnutrition - Hypokalemia - Lymphangioma - Pneumothorax - HIV - Hepatitis A - Optic neuritis 	<ul style="list-style-type: none"> - Liver abscess - Hypothyroidism - Pericardial effusion - Rubella - Acute periodontitis - Liver cell carcinoma - Neoplastic anaemia - Erythema nodosum - Malignant neoplasms - Diabetes insipidus - Chronic renal failure - Craniosynostosis - Keratoconjunctivitis - Laryngeal stenosis - Atrial septal defect
<ul style="list-style-type: none"> - Adrenocortical insufficiency - Congenital hypothyroidism - Disorders of protein metabolism (2) - Malignant neoplasm of the retina - Iron deficiency anaemia - Gastroenteritis and colitis (2) - Calcium metabolism disorder - Congenital laryngomalacia - Intracranial abscesses and granulomas - Craniopharyngeal tract neoplasms - Lepromatous leprosy - Acute upper respiratory tract infection - White blood cell disorders - Bile duct obstruction 	
Total	21

Table 5 shows the picture of SGPT test. Increased SGOT levels were found in all patients without comorbidities and 14 patients with comorbidities. In children without comorbidities, there was 1 patient whose SGPT increased and in children with comorbidities, there was an increase in SGPT in 11 patients.

Tabel 6 Overview of Albumin Tests

Albumin	N
Albumin Normal (>3,4 g/dL)	9
<ul style="list-style-type: none"> - Without comorbidities(2) - Pericardial effusion - Rubella - HIV - Hepatitis A - Liver abscess - Endometriosis - Anaemia - Hemorrhagic fever - Lymphangioma - Craniosynostosis - Hydrocephalus 	<ul style="list-style-type: none"> - Pneumonia - Laryngeal stenosis - Joint contractures - Septicaemia - Acute encephalitis - Liver cell carcinoma - Erythema nodosum - Malignant neoplasm - Pneumothorax - Conjunctivitis - Atrial septal defect - Acute periodontitis - Keratoconjunctivitis - Respiratory failure - Chronic renal failure - Acute upper respiratory tract infection - Intracranial abscesses and granulomas - Disorders of calcium metabolism - Lepromatous leprosy - Ventricular septal defect - Congenital laryngomalacia - White blood cell disorders - Ventricular septal defect
Albumin Low (<3,4 g/dL)	7
<ul style="list-style-type: none"> - Malnutrition (2) - Septic shock (2) - Pneumothorax - Optic neuritis - Diabetes insipidus - Jaundice - Malignant neoplasm - Acute renal failure - Ascites 	<ul style="list-style-type: none"> - Septicemia - Thrombocytopenia - Hypokalaemia - Down's syndrome - Tuberculosis - Neoplastic anaemia - Hypothyroidism - Hydrocephalus - Gastroenteritis and colitis - Bile duct obstruction - Cranio-pharyngeal tract neoplasms - Congenital hypothyroidism - Lymphoblastic leukaemia - Malignant neoplasm of the retina - Arterial embolism and thrombosis - Plasma protein metabolism disorders (2) - Adrenocortical insufficiency
Total	21

Table 6 shows the description of albumin test. A decreasing albumin level occurred in 7 patients (33.33%) and there was no decrease in albumin in patients without comorbidities.

Tabel 7 Overview of patient outcomes

Outcome	N	%
Died	4	19
<ul style="list-style-type: none"> - Hypothyroidism - Septic shock (2) - Optic neuritis - Tuberculosis - Hydrocephalus - Anaemia - Rubella - Septicaemia - Pneumothorax - Lymphangioma - Pneumonia 	<ul style="list-style-type: none"> - Malnutrition (3) - Acute encephalitis - Atrial septal defect - Diabetes insipidus - Respiratory failure - Hypokalaemia (2) - Liver cell carcinoma - Neoplastic anaemia - Malnutrition (3) - Craniosynostosis - Keratoconjunctivitis 	<ul style="list-style-type: none"> - Disorders of plasma protein metabolism (2) - Congenital laryngomalacia - Adrenocortical insufficiency - Arterial embolism and thrombosis - Cranio-pharyngeal tract neoplasms - Acute upper respiratory tract infection - Intracranial abscesses and granulomas - Gastroenteritis and colitis - Chronic renal failure - Pericardial effusion - Laryngeal stenosis
Recovered	17	21
<ul style="list-style-type: none"> - No comorbidities (3) - Jaundice - Conjunctivitis - Ascites - HIV - Liver abscess - Hepatitis A - Down's syndrome - Endometriosis - Erythema nodosum 	<ul style="list-style-type: none"> - Malignant neoplasm - Acute periodontitis - Acute renal failure - Hemorrhagic fever - Joint contracture - Thrombocytopenia - Neoplastic anaemia - Liver cell carcinoma - Congenital hypothyroidism 	<ul style="list-style-type: none"> - Bile duct obstruction - Iron deficiency anaemia - Plasma protein metabolism disorders (2) - Ventricular septal defect - Acute lymphoblastic leukaemia (2) - Malignant neoplasm of the retina - Lepromatous leprosy - Acute upper respiratory tract infection - Gastroenteritis and colitis - White blood cell disorders
Total	21	100

Table 7 describes the results of patient outcomes. Hepatitis B patients who died were 4 patients (19%) and recovered 17 patients (81%). In patients who died, there was an increase in SGPT and SGOT levels in 3 patients (75%), an increase in total bilirubin in 2 patients, an increase in recombinant bilirubin in 3 patients and a decrease in albumin in 2 patients.

4. Discussion

4.1 Demographics of Children's Patients

Based on the age of patients who have hepatitis B and its comorbidities who are inpatients and outpatients at RSUD Dr Soetomo Surabaya in this study, the age range is mainly 11-17 years, with an average patient age of 9.7 years, which is dominated by men. This is in accordance with the statement of Utsumi et al. (2010) that more children are detected with hepatitis B in children under 10 years of age, the majority of which are male children.

4.2 Liver Function and Serological Tests

Liver function test of patients with hepatitis B and its concomitants was performed to evaluate the status of hepatitis B in children. In the examination of SGOT found an increase in 17 patients and SGPT in 12 patients, in the examination of albumin found a decrease in 7 patients. Further monitoring of patients who have decreased albumin levels and increased SGOT and SGPT, this is done to prevent cirrhosis and hepatocellular carcinoma that can occur in these patients if they do not get the right therapy according to the conditions they experience. This is in accordance with research by Wang HB (2017) regarding ALT (SGPT) sensitivity to estimate the decrease in HBV DNA. This is in accordance with the results of research conducted by Sharma et al (2019) found an increase in SGOT and SGPT and a decrease in albumin levels in patients. In the serological examination of Anti-Hbe and Anti-HBc no data were obtained, in the examination of Anti-Hbs and HBeAg there were few examination results. In the HBV DNA examination, 1 data was obtained from 21 patients. This is in accordance with the research of Utsumi et al. (2010) showed that these children could have hidden hepatitis B infection.

4.3 Comorbidities of Children with Hepatitis B

There were 3 patients without comorbidities and the most common comorbidities were neoplastic anaemia and plasma protein metabolism disorders. Patients with elevated SGPT were found in 2 patients without comorbidities and 10 patients with comorbidities. In paediatric patients without comorbidities, there was no decrease in albumin levels and in children with comorbidities, there was a reduction in albumin levels and an increase in bilirubin rec and total levels influenced by comorbidities. This is in accordance with research by Fajrian (2020) who conducted research at Dr. H. Abdul Moeloek Hospital, Lampung Province, which showed an increase in total bilirubin levels along with an increase in SGOT and SGPT levels in patients with jaundice in accordance with the comorbidities suffered by the patient. similar things were found in the research of Handayani et al (2017) which showed an increase in SGOT and SGPT levels in dengue patients in accordance with the patient's comorbidities.

4.4 Outcomes of Children with Hepatitis B and Comorbidities

The outcome of hepatitis B patients with comorbidities was 4 patients who passed away

and 17 patients were cured. In patients who passed away, there was an increase in SGPT levels in 2 patients, SGOT in 3 patients and a decrease in albumin in 1 patient. This is influenced by comorbidities suffered by patients who affect and degrade the condition of children.

5. Conclusion

The conclusion of this study is that there is an increase in SGOT and SGPT in children without comorbidities and a decrease in albumin levels in paediatric patients with comorbidities. And in the results of patient outcomes for patients who died, it was found that the increase in SGPT, SGOT and decreased albumin levels in patients was influenced by the patient's comorbidities which caused the patient's condition to deteriorate.

Acknowledgements

Praise and gratitude to Almighty Allah for His blessings and grace, allowing us to complete a study entitled "Profile of Liver Function Tests, Serology and Demographic Status of Children with Hepatitis B and Comorbidities". We would also send our gratitude to child patients who became the research sample. Thereafter, we also acknowledge Prof. Dr. Aryati, dr., MS, Sp.PK(K), Ulfa Kholili, dr., Sp.PD, K-GEH, FINASIM and Dr. Bagus Setyoebodi, dr., SpA(K) for providing guidance in completing this study. Finally, we express our deepest thanks to our family for their endless love, help, and support.

References

- Dakl, A. A. A., & Alnuaimy, W. A. (2020). Epidemiology of Hepatitis B and C in Al-Muthanna Province. *Indian Journal of Forensic Medicine & Toxicology*, 14(2), 492–494. <https://doi.org/10.37506/ijfmt.v14i2.2851>
- Fajriani, F. M. (2020). Enzim Transferase dengan Bilirubin Total Penderita Ikterus Obstruktif Pendahuluan. *Jurnal Ilmiah Kesehatan Sandi Husada*, 11(1), 176–182. <https://doi.org/10.35816/jiskh.v10i2.240>
- Handayani, I., Indrati, A. R., & Alam, A. (2017). *Profil Manifestasi Klinis dan Laboratoris Pasien Dengue Bayi yang Menjalani Rawat Inap di RSUP. DR. Hasan Sadikin Bandung*. 19(3), 119–126.
- Jiang, M., Zhu, B., Yao, Q., Lou, H., & Zhang, X. (2021). Anti-HBs levels in children under the age of two years born to HBV carrier mothers after immunoprophylaxis: a multicenter cross-sectional study. *BMC Pediatrics*, 21(1), 1–7. <https://doi.org/10.1186/s12887-021-02967-8>
- Lee, W. M., King, W. C., Schwarz, K. B., Rule, J., & Lok, A. S. F. (2020). Prevalence and clinical features of patients with concurrent HBsAg and anti-HBs: Evaluation of the hepatitis B research network cohort. *Journal of Viral Hepatitis*, 27(9), 922–931. <https://doi.org/10.1111/jvh.13312>
- Lestari, C. S. W., Dewi, R. M., Sunarno, S., Hasugian, A. R., Handayani, S., Maha, M. S., Panjaitan, N. S. D., Ningrum, N., Sari, M., & Fairuza, F. (2023). The effectiveness of hepatitis B vaccine in toddlers based on the five-year period national basic health research (Riskesdas 2007, 2013 and 2018) in Indonesia. *PeerJ*, 11, e15199. <https://doi.org/10.7717/peerj.15199>
- Peng, T.-T., Cai, Q.-E., Yang, M., Chen, S.-P., Chen, F., Wang, M., Peng, L., Wong, G., Shen, C.-G., Cheng, W.-B., Liu, S.-Y., Peng, Y.-B., Peng, J.-H., Chen, C.-M., Yang, L.-Q., Tang, Y.-M., Xu, Z.-X., & Liu, Y.-X. (2019). Epidemiological trends and virological traits of hepatitis B virus infection in pregnant women and neonates. *Archives of Virology*, 164(5), 1335–1341. <https://doi.org/10.1007/s00705-019-04190-4>

- Pronocitro, C., Mulyani, N. S., Ghufron, A. A., Hazazi, Y. H., Ardianto, B., & Heriyanto, D. S. (2017). Efficacy of Hepatitis B Vaccination among Children in Special Region of Yogyakarta, Indonesia: Evaluation of Humoral and Cellular Immunity. *The Kobe Journal of Medical Sciences*, 63(3), E92–E98. <http://www.ncbi.nlm.nih.gov/pubmed/29434181>
- Rasmiatin, N, M. S., & Ekasari, T. (2023). Faktor Yang Mempengaruhi Status Imunisasi HB0 Pada Bayi Umur 0-7 Hari Di Wilayah Kerja Puskesmas Sukabumi. *Jurnal Ilmiah Obsgin*, 15, 223–235. <https://doi.org/https://doi.org/10.36089/job.v15i1.1042>
- Scheifele, D. W. (2019). Will Infant Hepatitis B Immunization Protect Adults? *Pediatric Infectious Disease Journal*, 38(6S), S64–S66. <https://doi.org/10.1097/INF.0000000000002326>
- Schillie, S., Vellozzi, C., Reingold, A., Harris, A., Haber, P., Ward, J. W., & Nelson, N. P. (2018). Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *Centers for Disease Control and Prevention*, 67(1), 1–31. <https://www.cdc.gov/mmwr/volumes/67/rr/tr6701a1.htm>
- Schollmeier, A., Glitscher, M., & Hildt, E. (2023). Relevance of HBx for Hepatitis B Virus-Associated Pathogenesis. *International Journal of Molecular Sciences*, 24(5), 4964. <https://doi.org/10.3390/ijms24054964>
- Stinco, M., Rubino, C., Trapani, S., & Indolfi, G. (2021). Treatment of hepatitis B virus infection in children and adolescents. *World Journal of Gastroenterology*, 27(36), 6053–6063. <https://doi.org/10.3748/wjg.v27.i36.6053>
- Utsumi, T., Yano, Y., Lusida, M. I., Amin, M., Hotta, H., & Hayashi, Y. (2010). *Serologic and Molecular Characteristics of Hepatitis B Virus among School Children in East Java, Indonesia*. 83(1), 189–193. <https://doi.org/10.4269/ajtmh.2010.09-0589>
- Yendewa, G. A., Lakoh, S., Yendewa, S. A., Bangura, K., Lawrence, H., Patiño, L., Jiba, D. F., Vandy, A. O., Murray, M. J. S., Massaquoi, S. P., Deen, G. F., Sahr, F., Hoffmann, C. J., Jacobson, J. M., Poveda, E., Aguilera, A., & Salata, R. A. (2021). Prevalence of hepatitis B surface antigen and serological markers of other endemic infections in HIV-infected children, adolescents and pregnant women in Sierra Leone: A cross-sectional study. *International Journal of Infectious Diseases*, 102, 45–52. <https://doi.org/10.1016/j.ijid.2020.09.1459>
- Zhang, X., Zhou, Y., Chen, C., Fang, W., Cai, X., Zhang, X., Zhao, M., Zhang, B., Jiang, W., Lin, Z., Ma, Y., Yang, Y., Huang, Y., Zhao, H., Xu, R., Hong, S., & Zhang, L. (2019). Hepatitis B virus reactivation in cancer patients with positive Hepatitis B surface antigen undergoing PD-1 inhibition. *Journal for ImmunoTherapy of Cancer*, 7(1), 322. <https://doi.org/10.1186/s40425-019-0808-5>