ORIGINAL ARTICLE

Serology Profile of Hepatitis B in Adolescents in Kupang, East Nusa Tenggara, Indonesia

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ABSTRACT

Introduction: Hepatitis B (HBV) infection rate dropped after Universal immunization program for infant launched. However, those persons who born before the program implemented may get HBV at a young age and susceptible to be infected. The present work aims to evaluate the epidemiology of HBV among the students of SMAN Kupang, East Nusa Tenggara. **Methods:** Total serum samples from 341 subjects, (ages 13-22, mean 17.5 \pm 1.69 years; male / female 133/208) have been tested for Surface antigen (HBsAg) and Surface Antibody (anti-HBs) and anti-core antigen (anti-HBc) for HBV. **Results:** HBsAg, anti-HBc, anti-HBs prevalence has been found 13.2%, 39.8%, 28.7%, respectively. It has been concluded that the percentage of young adults who are still vulnerable and at risk of contracting HBV is still high (52.7%). **Conclusion:** This study emphasizes the relevance of increasing the prevention strategy to filter out and to handle HBV carriers, including the implementation of screening for Hepatitis B and vaccine boosting that have been aimed at young adults.

Keywords: Hepatitis B, Serology Test, Adolescents, Kupang

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INTRODUCTION

World Health Organization (WHO) reported two billion people approximately found to having Hepatitis B virus (HBV) infection globally. Around 240 million chronic carriers may develop cirrhosis, liver failure and hepatocellular carcinoma (HCC) type of progressive disorders (1-4). More than 780,000 deaths resulted due to HBV infection every year. Hepatitis B infection is the main risk factor for liver cancer in developing countries (3, 4). HBV transmission needs to be prevented by vaccination, early detection as well as treatment of other diseased persons like patients on dialysis (5).

Hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), and antibodies to HBV core antigen (anti-HBc) have been carried out for HBV screening (6-8). HBsAg builds up excessively during the production of new viral particles, making HBsAg one of the best markers for HBV diagnosis (7-10). If the HBsAg persists more than 6 months or longer it is termed chronic hepatitis B (11-13). Anti-HB is also considered a conservative antibody, as it can neutralize HBsAg (10-11). Anti-HBs can be generated as a result of HBV vaccination (1,14). Indonesia is a moderate to a high endemic country for hepatitis B (1,15). The detection rate of HBsAg is different with a high prevalence in the East followed by the West throughout Indonesia (16, 17). It should be noted that Indonesia displays a very diverse ethnic background, a condition that supports the emergence of new HBV subgenotypes as well as unique HBV variants (17, 18). The national vaccination program in Indonesia started in 1997 (19). It is interesting to note these conditions and the challenges facing this vaccination program, with epidemiological studies on the young adult group born before and after program implementation. These people can be considered the "lost generation" when it comes to hepatitis B management. Adolescents become vulnerable to high HBV exposure risk due to their risky behavior (19).

The present work has been conducted to find out the epidemiology of HBV infection in the adolescents' population in Kupang with serological parameters. The findings demonstrate the HBV problem among adolescents in Indonesia. Present work will also provide practical information that can support the improving prevention, early detection and elimination of hepatitis B straggling in communities.

East Nusa Tenggara is a province with an archipelago, this makes East Nusa Tenggara a high transit area. Access to enter from other countries is also easy because East Nusa Tenggara is located in the same area as Timor Leste, can be reached by land access and also across the island from Australia. On one island, namely Rote Island, access from Australia can be reached by boat. The condition of high population movement can be an opportunity for a high spread of diseases, including Hepatitis B and AIDS.

Youth is the future of the nation, especially for the province of East Nusa Tenggara. Adolescence is the age where promiscuity is very high, the desire to try something new is also high, so this factor becomes one of the opportunities for spreading infectious diseases. The recent study is to obtain information regarding the description of the results of Hepatitis B serologic examination in high school students of Kupang by conducting HBsAg, Anti-HBs and Anti-HBc examinations using the ELISA Sandwich method.

MATERIALS AND METHODS

Samples

The sample of this study was venous blood from 341 students from SMAN 2, SMAN 3 and SMAN 4Kupang. Inclusion criteria were students who were not currently undergoing hepatitis B and C treatment and were willing to be included in the present work by signing informed consent. The exclusion criteria were students, diagnosed with HBV and HCV by a previous doctor and were not willing to be included in the study.

Serology Test

Examination to detect the presence of HBsAg, Anti HBs and Anti HBc was carried out using the Elisa immunoassays method (EvolisTM Biorad Laboratories, Inc., Hercules, CA).

Statistical analysis

Basic data are summarized descriptively. Results were analyzed by using the Statistical Package for Social Sciences v.20 (SPSS Inc., Chicago, IL). Correlations between serologic status and age, sex were evaluated through the Chi-square and Correlation test at the significance level of p < 0.05.

Ethical Permit

Ethical clearance has been obtained from the Health Research Ethics Commission of the Faculty of Medicine, University of Nusa Cendana vide number UN number-15050021. All subjects who have taken part in this study have been asked and signed the informed consent.

RESULTS

Examination of research samples was carried out from August to October 2020. Serological examinations were carried out at the Immunology Laboratory of the Medical Laboratory Technology Study Program, Poltekkes Kemenkes Kupang. The number of samples examined was 341 serums.

Demographic characteristics

Respondents' ages ranged from 13 years to 22 years with a median of 17.5 years (133 men and 208 women). The most ethnic groups that were respondents were the Timorese and Rote ethnic groups (Table I).

| Table I: Demographic | Characteristics | of | students | respondents | of |
|----------------------|-----------------|----|----------|-------------|----|
| SMAN in Kupang | | | | - | |

| Characteristics | n = 341 |
|--------------------|-----------------|
| Age | |
| Median | 17.5 years |
| Min-Max) (+ SD) | 13-22 years old |
| Male | 133 |
| Female | 184 |
| Race | |
| Timor | 50 |
| Flores | 9 |
| Rote | 51 |
| Belu | 6 |
| Sumba | 6 |
| Sabu | 14 |
| Alor | 3 |
| Etc | 179 |

Serological examination results

Serology examination includes testing for HBsAg antigen, testing for Anti-HBc and Anti-HBs antibodies. Serological examination result display the percentage of positive HBsAg was 13.2% (45 people), Anti-HBc 39.8% (136 people) and Anti-HBs was 98 people (28.7%) (Table II).

Table II: Results of HBsAg, Anti-HBc and Anti-HBs Serology Examination

| No. Inspection | | Posit | ive | Negative | |
|----------------|------------|-------|------|----------|-------|
| | Parameters | n | % | n | % |
| 1 | HBsAg | 45 | 13.2 | 296 | 86.8% |
| 2 | Anti-HBc | 136 | 39.8 | 205 | 60.1 |
| 3 | Anti-HBs | 98 | 28.7 | 243 | 71.2 |

A total of 45 people were positive for HBsAg, 32 people were positive for Anti HBc, 6 people were positive for AntiHBs and 12 people were HBsAg profiles. A total of 136 people were positive for AntiHBc, 32 positive for HBsAg, 104 negative for HBsAg, 80 positive for AntiHBs

and 51 people did not have AntiHBs. Of the 98 anti-HBs-positive subjects, 5 were HBsAg positive, 109 had anti-HBc, 27 had HBsAg and anti-HBc, and 12 were exclusively anti-HBs positive (Table III).

Relationship between gender and serology status

Furthermore, analysis of the relationship between sex and HBsAg, Anti-HBc and Anti-HBs serologic status was carried out. Table IV shows 26 (7.6%) men and 19 (5.6%) women were HBsAg positive. The analysis was continued with the chi-square test, the results showed a p value <0.05, meaning that there was a relationship between gender and HBsAg.

| PARAMETER | | | | | |
|-----------|----------|----------|----------------|------|--|
| | | | _ Total n % | | Interpretation |
| HBsAg | Anti-HBc | Anti-HBs | | | - |
| + | + | + | 5 | 1.5 | Chronic hepatitis B |
| + | + | - | 27 | 7.9 | Chronic hepatitis B |
| + | - | + | 1 | 0.3 | Possible HBsAg Mutations |
| + | - | - | 12 | 3.5 | HBsAg pos |
| - | + | + | 80 | 23.5 | Recovering from infection |
| - | + | - | 24 | 7.0 | It is possible that Hep B is hidden |
| - | - | + | 12 | 3.5 | Immunity induced by vac- cines |
| - | - | - | 180 | 52.8 | Potential for infection |
| Total | | | 341 | 100 | |

Table III: Clinical Interpretation based on Serological examination

Table IV: Analysis of the Relationship between Gender and HBsAg status

| | | HBs | Ag status | Total | |
|--------|--------|------------|-------------|-------------|--|
| | | Positive | Negative | Total | |
| C I | Male | 26 (7.6%) | 112 (32.8%) | 138 (40.5%) | |
| Gender | Female | 19 (5.6%) | 184 (54%) | 203 (59.5%) | |
| Total | | 45 (13.2%) | 296 (86.8%) | 341 (100%) | |

DISCUSSION

Hepatitis B is a major health problem worldwide and the distribution of cases is uneven, with most of the endemic areas located mostly in LMICs Asia and Africa (1, 2, 20). Hepatitis B prevention has been focused on infant immunization programs. The program was implemented among 183 members of World Health Organization (WHO) which includes Indonesia (1, 21). This program succeeded in reducing the prevalence of hepatitis B (22-24). However, it will take around 15-20 years to get the protection of the entire community using this strategy itself (25-26). Susceptibility to HBV infection of teenagers will remain who born before the initiation of universal infant immunization program; many affected by the disease in childhood and be at risk to develop the advanced chronic disease later in life (2, 27). In this age group, while they are included in the group that entered the adult community and may be involved in activities resulting to be infected with HBV (2, 31, 26).

Significant socioeconomic burdens, with the loss of individuals who are working effectively and increased health-related costs, arise from chronic liver disease (30, 26). They also play an important role in the spreading of HBV throughout their life, from parent to child vertically, and to society horizontally (19, 25-28). The present work aims to analyze the burden of disease in young adults in Kupang and its implications as input in the management of HBV.

Parameters associated with HBV infection were associated with men and the aged person reported earlier (30, 31). Results showed a high prevalence of hepatitis B with an HBsAg detection rate of 13.2%. In addition, the prevalence of anti-HBc indicated that more than one-third (39.8%) having Hepatitis B. Whereas, anti-HBs has occurred among only 28.7% of a study group. 76.6% of which has concurrent with anti-HBc, indicating exposure and resolution rather than immunization. These findings suggest an increased rate of infection among the studied population.

Hepatitis B detection using molecular methods, namely PCR is the gold standard method which is considered very accurate and effective. However, their use for mass screening may raise hurdles in terms of cost and time compared to serological testing (25-27). Therefore, in an endemic country like Indonesia, it still makes more sense to use HBsAg as the initial parameter for HBV detection, in addition to anti-HBc. The epidemiological data obtained in the present work establish an initial assessment of the magnitude of the challenges that should be considered for expanding the national immunization program (28-30).

Hepatitis B protection has been reported a very low prevalence of isolated anti-HBs (3.5%). This reaffirms the need for a complete booster dosage of vaccination among adolescents and young adults, who are with a seronegative status (1, 2, 25). As per WHO guidelines and recommendation administration of this vaccine is an addition to routine infants (26, 31, 32). Our research provides recommendations for the government to provide free vaccinations to young adolescents who are at high risk of exposure.

CONCLUSION

The present study establishes among the young adult population in Kupang, Indonesia a higher rate of infection of HBV with the parameters HBsAg (13.32%), Anti-HBs (39.9%) and Anti-HBs (36.6%). A major percentage of the population studied shows susceptibility to HBV infection (52.7%), which indicates the need for increased public awareness and the importance of catching up or increasing HBV vaccination. The results of this study emphasize the need to improve preventive procedures for screening and managing HBV carriers, including implementation of vaccination especially for high-risk target populations such as adolescents and young adults.

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REFERENCES

- 1. WHO. Hepatitis B fact sheet no. 204. 2015 [cited Dec 30, 2020]. Available from: http://www.who. int/mediacentre/factsheets/fs204/en/.
- 2. WHO. Guidelines for the Prevention, Care and Treatment of Persons with Chronic Hepatitis B Infection. 2015; Geneva, Switzerland: WHO Press.
- 3. Akinyemiju T, Abera S, Ahmed M, Alam N, Alemayohu MA, Allen C, et al.; Global Burden of Disease Liver Cancer Collaboration. The Burden of Primary Liver Cancer and Underlying Etiologies From 1990 to 2015 at the Global, Regional, and National Level: Results From the Global Burden of Disease Study 2015. JAMA Oncol. 2017; 3(12):1683–91.
- 4. Liu Z, Jiang Y, Yuan H, Fang Q, Cai N, Suo C, et al. The trends in incidence of primary liver cancer caused by specific etiologies: results from the Global Burden of Disease Study 2016 and implications for liver cancer prevention. J Hepatol. 2019 Apr;70(4):674–83.
- Irfan, I., Wawomeo, A., & Kambuno, N. T. Hepatitis B Virus Infection in Hemodialisis patient at Prof. DR. WZ Johannes Kupang Hospital, East Nusa Tenggara. Jurnal Kesehatan Primer, 2019;4(1): 63-69.
- 6. Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., ... & Remuzzi, G. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. The lancet, 2012; 380(9859): 2095-2128.
- 7. Bowden, S. Laboratory diagnosis of hepatitis B infection. United Kingdom: International Medical Press Ltd. 2002;145-160.
- Kambuno NT, Sari A, Nurdin KE, Novicadlitha Y, Siregar I. The relation of blood donors' characteristic toward prevalences of HBsAg and Anti-HCV on blood transfussion unit of PMI in Province of East Nusa Tenggara. InProceeding 1st. International Conference Health Polytechnic of Kupang 2018 Dec 31 (pp. 303-310).
- Kambuno NT. , Djuma Agustina W. , Barung Elisabeth N. , Siregar Irma, Risk factor for hepatitis B family transmission in Kupang province of East Nusa Tenggara, Indonesia, Pak. J. Med. Health Sci. 2020; 14 (2): 1425-142810. Kann M., "Structural

and molecular virology. Lai CL, Locarnini S, eds. Hepatitis B Virus. London", United Kingdom: International Medical Press Ltd., 2002; 9–22.

- 11. EASL.,"EASL clinical practice guidelines: management of chronic hepatitis B virus infection" J Hepatol, 2012; 57: 167–185.
- 12. Liaw YF, Kao JH, Piratvisuth T, Chan HL, Chien RN, Liu CJ, Gane E, Locarnini S, Lim SG, Han KH, Amarapurkar D. Asian-Pacific consensus statement on the management of chronic hepatitis B: a 2012 update. Hepatology international. 2012 Jun; 6(3):531-61
- 13. Lok, A. S., & McMahon, B. J. Chronic hepatitis B: update 2009. Hepatology, 2009; 50(3), 661-662.
- 14. Schillie, S. F., & Murphy, T. V. Seroprotection after recombinant hepatitis B vaccination among newborn infants: a review. Vaccine, 2013; 31(21): 2506-2516.
- Khan, M., Dong, J. J., Acharya, S. K., Dhagwahdorj, Y., Abbas, Z., Jafri S. M, W., ... & Sarin, S. K. Hepatology issues in Asia: perspectives from regional leaders. Journal of Gastroenterology and Hepatology, 2014;19: S419-S430.
- Tsuda, F., Karossi, A. T., Soewignjo, S., Sumarsidi, D., Trisnamurti, R. H., Udin, L. Z., ... & Mishiro, S. Distribution of the hepatitis B surface antigen subtypes in Indonesia: implications for ethnic heterogeneityand infection control measures. Archives of virology, 1997 Nov 1; 142(11): 2121-9.
- 17. Thedja, M. D., Muljono, D. H., Nurainy, N., Sukowati, C. H., Verhoef, J., & Marzuki, S. Ethnogeographical structure of hepatitis B virus genotype distribution in Indonesia and discovery of a new subgenotype, B9. Archives of virology, 2011 May;156(5): 855-868.
- Lusida, M. I., Nugrahaputra, V. E., Handajani, R., Nagano-Fujii, M., Sasayama, M., Utsumi, T., & Hotta, H. Novel subgenotypes of hepatitis B virus genotypes C and D in Papua, Indonesia. Journal of clinical microbiology, 2008; 46(7): 2160-6.
- 19. Herawati, M. H. Program pengembangan imunisasi dan produk vaksin hepatitis B di Indonesia. Cermin Dunia Kedokteran, 1999; 124: 25-27.
- 20. Putriyanti, C. E., & Ratnawati, E. Normal Puberty Knowledge and Adolescent Menstrual Cycles. Jurnal Info Kesehatan, 2019;17(2): 119-133.
- 21. Lavanchy, D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. Journal of viral hepatitis, 2004; 11(2): 97-107.
- 22. Hsu, H. Y., Chang, M. H., Liaw, S. H., Ni, Y. H., & Chen, H. L. Changes of hepatitis B surface antigen variants in carrier children before and after universal vaccination in Taiwan. Hepatology, 1999; 30(5): 1312-1317.
- 23. Oon, C. J., Goh, K. T., & Lim, G. K. Clearance of neonatal antiHBc following hepatitis B vaccination: relationship to antiHBs levels. Annals of the

Academy of Medicine, Singapore, 1991; 20(2): 231-235.

- Ruff, T. A., Gertig, D. M., Otto, B. F., Gust, I. D., Sutanto, A., Soewarso, T. I., ... & Maynard, J. E. Lombok Hepatitis B Model Immunization Project: toward universal infant hepatitis B immunization in Indonesia. Journal of Infectious Diseases, 1995;171(2): 290-6.
- 25. Bonanni, P. Universal hepatitis B immunization: infant, and infant plus adolescent immunization. Vaccine, 1998; 16: S17-S22.
- Brookman, R. R., Koff, R. S., Schaffner, W., Margolis, H. S., Collins, M., Bloom, B. S., & Coupey, S. M. Critical issues surrounding hepatitis B vaccination for adolescents: a roundtable. Journal of Adolescent Health, 1995; 17(4): 208-233.
- 27. Cassidy, W. M., & Mahoney, F. J. A hepatitis B vaccination program targeting adolescents. Journal of adolescent health, 1995; 17(4): 244-7.

- 28. Abdel-Hady, M., & Kelly, D. Chronic hepatitis B in children and adolescents: epidemiology and management. Pediatric Drugs, 2013; 15(4): 311-7.
- 29. de Paula Machado, D. F. G., Martins, T., Trevisol, D. J., e Silva, R. A. V., Narciso-Schiavon, J. L., Trevisol, F. S., & de Lucca Schiavon, L. Prevalence and factors associated with hepatitis B virus infection among senior citizens in a Southern Brazilian city. Hepatitis Monthly, 2013;13(5); .
- Stepień, M., & Czarkowski, M. P. Hepatitis B in Poland in 2011. Przeglad epidemiologiczny, 2013; 67(2): 239-45.
- 31. Shouval, D. Is universal vaccination against hepatitis B sufficient for control of HBV infection? Lessons from the immunization campaign in Italy. Journal of hepatology, 2000;33(6): 1009-11.
- 32. Wait, S., & Chen, D. S. Towards the eradication of hepatitis B in Taiwan. The Kaohsiung journal of medical sciences, 2012;28(1): 1-9.