BERKELEY PUBLICATION
AND RESEARCH INTERNATIONAL
12.31.2020
Journal of Med., Biological and Pharm. Sci. Vol. 14 No. 3

HEPATITIS B VIRUS (HBV) AND PLASMODIUM CO-INFECTION IN ASYMPTOMATIC CASES

GINSAU, M. A[1] AND AHMED, U.A[2]

[1]Department of Science Laboratory Technology, School of Science and Technology, Jigawa State Polytechnic, Dutse, Nigeria [2]Department of Biological Science, Federal University, Gashua, Yobe State, Nigeria

ABSTRACT

Co-infection of hepatitis B virus and Plasmodium are likely happening in communities and to our knowledge, no investigation is done to realize it. This is likely happening among asymptomatic individuals. Asymptomatic stage serves as reservoir for re-start of transmission in areas where a disease is eradicated and it may progress to acute and chronic conditions. This study seeks to investigate the incidence of co-infection of the two pathogens considering their medical importance. Sero-chromatographic immunoassay method was employed in this study and result revealed 30% incidence. This is for a small population, 100 persons and one method was employed, we therefore, recommend for this kind of investigation in a larger population by multiple investigation methods such as liver biopsies, ultrasound, nucleic acid testing, among others.

Introduction:

Viral hepatitis is the most common type of hepatitis worldwide. Viral hepatitis is caused by five different viruses (hepatitis A, B, C, D, and E) (Dienstang, 2015). Worldwide in 2005, chronic hepatitis B affected about 343 million people. Hepatitis results in more than a million deaths a year, most of which occur indirectly from liver scarring or liver cancer (Lancet, 2016). Hepatitis B is transmitted when blood or mucous membranes are exposed to infected blood and body fluids, such as semen and vaginal secretions. Viral particles have also been found in

ISSN: 1211-4401

Keywords: *Asymptomatic, Co-infection, Hepatitis, Plasmodium, Virus*

Saliva and breast milk. However, kissing, sharing utensils, and breastfeeding do not lead to transmission unless these fluids are introduced into open sores or cut (Dienstag, 2015). Close to 780,000 deaths in the world are attributed to hepatitis B. Hepatitis accounts for much larger, percentage of health care spending in endemic regions like Asia (Chan and Jia, 2011). In 1997 it accounted for 3.2 of South Korea's total health care expenditures and resulted in $696 million in direct costs. A large, majority of that sum was spent on treating disease symptoms and complication (Lavanchy, 2004). Chronic hepatitis B infections are not as endemic as in the United States, but accounted for $357 million hospitalization costs in the year 1990 (Udompap et al., 2015). That number grew to $1.5 billion in 2003, but remained stable as of 2006, which may be attributed to the introduction of effective drug therapies and vaccination campaigns (Lemoine et al., 2014). On the other hand, malaria is a major global public health problem and a leading cause of morbidity and mortality in many countries. Malaria caused an estimated 219 (range 154 – 289) million cases and 660,000 (range 490,000 – 836,000) deaths in 2010. Approximately 80% of the cases and 90% of the deaths occur in Africa while the remaining cases and deaths occur mainly in the South-East Asia and Eastern Mediterranean Regions (W.H.O, 2012).

Parasitic hepatitis is caused by different group of parasites. Of protozoans, Trypanosoma cruzi, Leishmania species, Entamoeba histolytica, and the malaria-causing Plasmodium species all can cause liver inflammation. Parasites can infect the liver and active the immune response, resulting in symptoms of acute hepatitis with increased serum IgE (though chronic hepatitis is possible with chronic infections) (Harder and Mehlhom, 2008). Of the worms, the cestode Echinococcus granulosus, also known as the dog tapeworm, infects the liver and forms characteristcs hepatic hydatid cysts (Harder and Mehlhom, 2008). The liver flukes Fasciola hepatica and Clonorchis sinensis live in the bile ducts and cause progressive hepatitis and liver fibrosis.

The pathway by which hepatic virus cause viral hepatitis is best understood in the case of hepatitis B and C. The viruses do not directly cause cell death. Rather, infection of liver cells activates the innate and adaptive arms of the immune system leading to an inflammatory response which causes cellular damage and death (Nakamoto and Kaneco, 2003). Depending on the strength of the immune response, the types of immune cells involved and the ability to evade the body's defense, infection can either lead to clearance (acute disease) or persistence (chronic disease) of the virus. The chronic presence of the virus within liver cells results in multiple waves of inflammation, injury and wound healing that overtime lead to scarring or fibrosis and culminate in hepatocellular carcinoma (Wong, 2014). Individuals with an impaired immune response are at greater risk of developing chronic infection. Natural killer cells are the primary drivers of the initial innate response and create a cytokine environment that results in the recruitment of CD4 T-helper and CD8 cytotoxic T-cells (Wong, 2014).

Plasmodium first enters the liver cells to undergo pre-erythrocytic schizogony before invading the red blood capsules (Jordan and Verma, 2011). Acquired immunity in malaria involves both humoral and cellular immunity. Antibodies against sporozoites and sexual and asexual blood stages develop in malaria patients. A variety of cellular mechanisms may play role in conferring protection against malaria. These include natural killer activity and activated macrophages. The latter phagocytes and induce extracellular killing of target cells. Immunity produced following infection with malaria parasites is species specific, stage-specific and strain- specific and the immunity lasts only till original infection remains active. This is known as concomitant immunity. Plasmodium antigens on the infected red cell surface are targets for naturally acquired immunity to malaria. Plasmodium falciparum erythrocyte membrane protein 1 (PfMP1) is a potentially important family of target antigens, because these proteins are inserted into the red cell surface and are prominently exposed and because they are highly polymorphic and undergo clonal antigenic variation. The apparent selective pressure exerted by established anti-

PfMP1 antibodies on the infecting parasite supports the idea that such responses provide variant-specific protection against the infection (Peter et al., 1998).

Diagnosis of hepatitis is made on the basis of some or all of the following: a patient's signs and symptoms, medical history including sexual and substance use history, blood tests, imaging, and liver biopsy (Friedman, 2015). Blood testing includes liver enzymes, serology, nucleic acid testing (for hepatitis virus DNA/RNA), blood chemistry, and complete blood count. Characteristics patterns of liver enzyme abnormalities can point to certain cause or stages of hepatitis (Green and Flamm, 2002). Generally, AST and ALT are elevated in most cases of hepatitis regardless of whether the patient shows any symptom. However, the degree of elevation, the predominance for AST versus ALT elevation, and the ratio between AST and ALT are informative of diagnosis (Friedman, 2015).

Ultrasound, CT, and Magnetic Resonance Imaging can all identify steatosis (fatty changes) of the liver tissue and nodularity of the liver surface suggestive of cirrhosis. These are able to provide a higher level of detail, allowing visualization and characterize such structures as vessel and tumors within the liver (Sahani and Kalva. 2004).

Enzyme-linked Immunosorbent Assay (ELISA) has been a valuable tool in epidemiological studies and in assessing the risk and identification of plasmodium. The antigen panel assay is the rapid wicking assay that identifies the presence or absence of Plasmodium. The assay is rapid, one strip, one step procedure using wicking test strip. Rapid results, ambient storage and lack of specialized equipment needed in testing samples are big advantages of wicking ELISA.

Both viral hepatitis and malaria have similar clinical manifestations and their causative agents attack liver. These include fatigue, nausea, vomiting, poor appetite joint pain, fever and headaches. People can experience liver-specific symptoms including choluria (dark urine) and clay-coloured stool. The non-specific symptoms in the prodromal typically resolve by this time, but people will develop an enlarged liver and right upper abdominal pain or discomfort (Dienstag, 2015).

Asymptomatic hepatitis B virus patients have no present/past symptoms or signs of liver disease and have HBsAg positivity on two occasions more than six months apart (Dixit and Jena, 2008). The precise monitoring of asymptomatic individuals and submicroscopic cases of malaria through molecular assays and valid serological methods, especially in regions where seasonal and low transmission exists can be very helpful at this phase (Gholmreza et al., 2017).

Co-infection is the simultaneous infection of a host by multiple pathogen species. In virology, co-infection includes simultaneous infection of a single cell by two or more virus particles. An example is the co-infection of liver cells with hepatitis B virus and hepatitis D virus which can arise incrementally by initial infection followed by super infection (Cox, 2001). There are few investigations on co-infection worldwide and there is none for Hepatitis B virus and Plasmodium, therefore, this research has investigated the incidence of co-infection of the two pathogens.

Materials and Method

One hundred persons who had not present clinical symptoms of hepatitis and malaria were subjected to this study. Their blood samples were examined for Hepatitis B virus and Plasmodium and this was achieved by Sero-chromatographic immunoassays for qualitative detection of HBsAg and wicking Test Strip for Plasmodium antigen. The assays were rapid, one strip, and one step.

Results

Table 1: The Status of 100 Asymptomatic Individuals with Respect to Hepatitis B virus and Plasmodium

Asymptomatic individual	Percentage Asymptomatic %	Agent (s)/Type of Infection
30	30%	Co-infection *
17	17%	Hepatitis B virus only
53	53%	Plasmodium only
100	**100**%	

Legend: * = Hepatitis B virus and Plasmodium in a single individual

Discussion

Asymptomatic means of a condition or person producing or showing no symptom. Asymptomatic means there are symptoms you are considered asymptomatic if you: Have recovered from an illness or condition and no longer have symptoms. Have illness or condition and no longer have symptoms. Have illness or conditions such as early stage (Medline, 2019). Ours are those that show no symptom and do not present themselves to clinic.

Global prevalence or incidence of co-infection among human is unknown, but it is thought to be commonplace (Cox, 2001), sometimes more common than single infection (Petney and Andrews, 1998). The positive finding of this study seems a kick-off of prevalence study of co-infection most especially with regards to Hepatitis B virus (HBV) and Plasmodium. It presents 30% cases of co-infection and it proves that the infection is commonplace. In addition to the above, it presents two pathogens of different species interacting within one host as suggested by Griffiths et al. (2011) that co-infection is of particular human importance because pathogen species can interact within the host.

The finding of this study is the first one ever on co-infection of HBV and Plasmodium, others were reported on tuberculosis and HIV, HVB and HDV, in which W.H.O (2011) reported a globally common co-infection involves tuberculosis and HIV in some countries, up to 80% of tuberculosis, patients are also HIV positive. Co-infection increases with the rate of fulminant hepatitis from 1% in regular HBV to 4% in patents co-infected with HBV and HDV (W.H.O., 2011).

Asymptomatic malaria reservoirs are more than they were believed to be. Individuals that can be diagnosed with microscopic or submicroscopic methods have microscopic gametocyte density and Bousema et al. (2014) believed that, in order to eliminate malaria. Interventions should target both symptomatic and asymptomatic infections. In regions where there is seasonal and low transmission of malaria even a small percentage of

infected persons are sufficient to re-start malaria transmission. In this study, we suggested that the 53% of asymptomatic Plasmodium case is reservoir for next stage of disease manifestation (symptomatic) and suggests for immediate co-infection with HBV.

In the other way round, the 17% asymptomatic HBV is probably becoming co-infected with Plasmodium. Probably infected asymptomatic individual can become a source of parasitic transmission to health individuals under favourable settings considered a settings considered a serious challenge to malaria control and elimination worldwide (Lin et al., 2014).

The popular belief is that in low transmission setting the proportion of asymptomatic individuals is less than that in areas of greater transmission severity. However, community-based structures have shown that, although an increased transmission state is associated with an increase in the reservoir share, but even in low transmission areas the asymptomatic cases make up for 60% of infected population (Sturrock et al., 2013). Therefore, it seems that in low transmission settings malaria infection is very likely to be asymptomatic (W.H.O., 2013). Based on the above explanation, we predict that the 30% co-infection may increase as the population increased.

The extent of asymptomatic condition according to this study could be due to incubation period. The incubation period of HBV infection is 40 – 150 days. The clinical illness assorted with acute HBV infection may range from mild disorders. After hepatitis resolves, 95%of adult patients and 5 – 10% of infected in infants ultimately develop antibodies against HB surface antigen that is, anti-HBS-clear HBsAg (and HBV), and fully recover.

Conclusion

This study reported 30% co-infection of Hepatitis B virus and Plasmodium among 100 asymptomatic individuals.

References

Bousema,T., Okell, L., Felger, I., and Drakely, C. (2014). Asymptomatic malaria Infections: Detectability, Transmissibility and Public Health Relevance. Nature Rev Microbiol. 12(12):823 – 840

Chan, H.L., and Jia, Jidong (2011). ''Chronic hepatitis B in Asia – new insights from the past decade'' Journal of Gastoenterology and Hepatology, **26**:131 – 137

Cox, F. E. (2001). "Concomitant infections, parasites and immune responses". Parasitology. 122 Supplement: S23 - 38

Dienstag, J.L. (2015). ''Acute Viral Hepatitis''. Harrison's Principles of Internal Medicine, New York, McGraw-Hill, 9th edition Friedman, L. S (2015). Current Medical Diagnosis & Treatment 2016. McGraw Hill. Chapter 16

Dixit, V.K and Jena, S.K. (2008). Incidentally Detected Asymptomatic HBsAg positive subjects. Hepatitis B Annual 2008; 5: 95 – 101

Friedman, L.S. (2015). ''Liver, Biliary Tract, & Pancreas Disorders''. In Papadakis, M; McPhee, S.J., Rabow, M.W. Current Medical Diagnosis & Treatment 2016 55e. McGraw Hill

Gholmreza, H., Mehdi, M., Hojjat, Z., Ahmad, R., and Hussein, K. (2017). Asymptomatic Malaria and its Challenges in Malaria Elimination Programme in Iran: A systemic Review. Journal of Arthropod Borne Diseases.

Green, R.M. and Flamm, S. (2002). "AGA Technical Review on the Evaluation of Liver Chemistry Tests". Gastroenterology. **123**(4): 1367 – 84

Griffiths, E. C., Pedersen, A.B.P., Fenton, A., and Petchy, Q.P (2011). The nature and consequences of co-infection in Humans. Journal of Infection. 63 (3): 200 - 206

Harder, A., Mehlhom, H. (2008)." Diseases Caused by Adult parasites or Their Distinct Life Cycle Stages". In Weber, O., and Protzer, U. Comparative Hepatitis. Birkhauser. Pp161 – 216

Jordan, E.L. and Verma, P.S. (2011). Invertebrate Zoology. S. Chad & Company Ltd, Ram Nagar, New Delhi, India. pp 176 – 925.

Lavancy, D. (2004). " Hepatitis B virus Epidemiology, Disease Burden, Treatment, and Current Emerging Prevention and Control Measures". Journal of Viral Hepatitis. **11**(2):97 – 107.

Lemoine, M, Eholie, S., and Lacombe, K. (2014). "Reducing the neglected Burden of Viral Hepatitis in Africa: Strategies for a Global Approach". Journal of Hepatology. **62** (2): 469 – 476.

Lin, J.T., Saunders, D.L., and Meshnick, S.R. (2014). The Role of submicroscopic Parasite Mia in Malaria Transmission: What is the Evidence? Trends Parasitol. 30(4):183 – 190

Medline Plus (2019). Glossary of Diabetes, Medically Reviewed. Medline Plus.gov Retrieved on 02/17/2019

Nakamoto, Y. and Kaneko, S (2003). "Mechanisms of viral hepatitis induced liver injury Current Molecular Medicine. **3** (6): 537 – 544

Petney, T. N. and Andrews, R. H, (1998)."Multiparasite communities in animals and humans: Frequency , Structure and Pathogenic significance". International Journal of Parasitology, **28** (3): 377 – 393

Sahani, D.V. and Kalva, S. P. (2004). "Imaging the Liver". The Oncologists, 9 (4):385-97

Sturrock, H.J . and (2013). Targetting Asymptomayic Malaria Infections: Active Surveillance In control and elimination. Plos Med. 10 (6): e1001467

Udompap, P., Kim, D. and Kim, W.R.(2015). "Current and Future Burden of Chronic Non Malignant Liver Disease". Clinical Gastroenterology and Hepatology; 13(12) 2031 – 2041