

Prevalence and Risk Factors of Hepatitis B among Pregnant women attending antenatal clinics in Abuja Nigeria.

Laura Madukaji, Ifeanyi Ossamulu, Grace Mambulla, Musa Galadimma, Faruk Kuta

ABSTRACT

Nigeria is one of the countries considered as a highly endemic country for hepatitis B, mainly due to perinatal transmission of hepatitis B virus (HBV). The prevalence of HBV surface antigen (HBsAg) carriage in pregnant women is a relevant marker for the risk of mother-to-child HBV transmission. This study was conducted to determine the prevalence of Hepatitis B virus infection among pregnant women visiting antenatal clinics in Abuja Nigeria. A total of 350 pregnant women were screened for hepatitis B virus surface and core antibodies. Out of the screened women, 34(9.7%) were positive for HBsAg while 10(2.9%) were positive for HBcAb. Pregnant women within the age group 25-29 years recorded prevalence of 3.7% HBsAg while 30-34 years had 1.4% HBcAb. Pregnant women with and without history of surgery had prevalence of 4.86% each for HBsAg and 1.43% HBcAb. Pregnant women that share sharp objects had prevalence of 3.43% for HBsAg and 1.14% for HBcAb compared to others. Pregnant women from polygamous homes had a prevalence of 1.7% for HBsAg and 0.29% for HBcAb while women from monogamous had 8% for HBsAg and 2.57% HBcAb. Prevalence of 8.57% for HBsAg and 2.86% for HBcAb was recorded for pregnant women that are non health workers while 1.14% HBsAg only was recorded for health workers. Pregnant women with history of blood transfusion had prevalence of 8% for HBsAg and 2.3% HBcAb while women without history of blood transfusion had prevalence of 1.71% for HBsAg and 0.57% for HBcAb. Statistical analysis (chisquare, t- test and correlation regression) showed no significant relationship between the rates of infection with hepatitis B virus and socio economic factors considered except in age group. HBsAg prevalence observed in pregnant women in Abuja, Nigeria reflects a high risk of HBV perinatal transmission and call for a widespread action for the newborns.

KEYWORDS: Hepatitis B Virus, Serological markers, Ante natal clinics, Abuja, Nigeria

INTRODUCTION

The liver which is a vital organ that processes nutrients, filters the blood, fights infections can be inflamed or damaged when its function is affected (Santos, Choquette and Bezerra, 2010). Hepatitis is a general term referring to inflammation of the liver, which may result from various causes (Ghabril, Chalasani and Björnsson, 2010). Hepatitis can be caused by both infectious (i.e. viral, bacterial, fungal, and parasitic organisms) and non infectious agents (e.g. alcohol, drugs, autoimmune diseases, and metabolic disorders) but viral hepatitis are the most common cause of hepatitis worldwide (Malaguarnera, Cataudella, Giordano, Nunnari, Chisarin and Malaguarnera, 2012). The most common causes of viral hepatitis are these hepatotropic viruses; Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D and Hepatitis E (Gallegos-Orozco, Rakela-Brödner, and Gross, 2010). Other viruses can also cause liver inflammation such as Herpes Simplex, Cytomegalovirus, Epstein-Barr virus or Yellow fever (Naides, 1998).

Hepatitis B virus is a hepadnavirus that has a circular genome of partially double-stranded DNA and replicates through an RNA intermediate form by reverse transcription, it was originally known as "serum hepatitis" (Bartenschlager, Junker-Niepmann, Schaller, 1990). The virus can remain viable for more than 7 days on environmental surfaces at room temperature. The average incubation period is 90 days from time of exposure to onset of symptoms, but may vary from 6 weeks to 6 months.. Hepatitis B virus is a major global health problem that can cause chronic liver disease and put people at high risk of death from cirrhosis of the liver and liver cancer. More than 240 million people have chronic (long-term) liver infections and more than 780,000 people die every year due to acute or chronic consequences of hepatitis B (Santos *et al.*, 2010).

Perinatal infection is a major route of infection in developing countries, about 10-20% of seropositive women transmit the virus to their neonates in the absence of immunoprophylaxis (Okonko, Okerentugba and

Innocent-Adiele, 2012). A newborn baby can get the virus from the mother during delivery when the baby comes in contact with the mother's body fluids in the birth canal (Lee, Lo, Tsai, Wu, Wu, Yang, and Ng, 1998). In women who are seropositive for both HBsAg and HBeAg vertical transmission is approximately 90% (Leung, 2009). In patients with acute hepatitis B, vertical transmission occurs in up to 10% of neonates when infection occurs in the first trimester and in 80 -90% of neonates when acute infection occurs in the third trimester (Xu, Yan, and Choi, 2002).

Diagnosis of hepatitis is made by biochemical assessment of liver function (Mast, Weinbaum and Fiore, 2006). Initial laboratory evaluation should include: total and direct bilirubin, Alanine transferase, Aspartate ,prothrombin time, total protein, albumin, serum globulin, complete blood count, and coagulation studies. Diagnosis is confirmed by demonstration in sera of specific antigens and/or antibodies (Aspinall, Hawkins, Fraser, Hutchinson and Goldberg, 2011). Tests specific for complete virus particles in liver and serum are available only in research laboratories (Zoulim, 2006).

Serological markers are key elements in diagnosing acute hepatitis B virus (HBV) infection and determining its possible evolution towards chronicity (Lee, 1997). Serologic testing for the diagnosis of hepatitis B virus (HBV) infection involves measurement of a panel of distinct HBV-specific antigens and antibodies reaction (Linnen, Wages and Zhang-Keck, 1996). The panel of responses can determine whether a patient is susceptible to infection, immune as a result of resolved infection, immune as a result of vaccination, acutely infected, or chronically infected. The primary markers are HBsAg, HBeAg, Anti-HBc, Anti-HBe, Anti-HBs. The limitation in the diagnosis is that once treatment of chronic HBV is initiated with approved anti-hepadnaviral agents, the measurement of HBV DNA in serum can only be done with molecular technology, which helps monitor treatment efficacy but also indicates breakthrough infection should drug resistance emerge (Chang and Lewin, 2007). Advances in the molecular diagnosis of drug resistance using highly sensitive methodologies such as DNA hybridization assays can further pinpoint the type of mutation responsible and, more importantly, detect upcoming viral resistance at an early stage when the variant represents only a minor fraction of the total viral population. Such new tools are especially relevant for patients at high risk for disease progression but are

expensive (Cindy, Weinbaum, Ian, Eric, Mast, Susan,... Ward, 2008)

Statement of the Research Problem

Hepatitis B Virus can be transmitted from one generation to another during child birth and has been reported to be a major cause of death in time past. It affects the most sensitive organ of the body. To date, transmission and management of Hepatitis B is an issue of medical importance.

Justification of the Study

Studies (Seyed, Azar, Kourosh, Mohammad, Hamid and Mohammad, 2011) have been done on Hepatitis B Viral infection in different parts of the world but information regarding the prevalence of HBV infection in pregnant women using two serological markers (HBsAg and HBcoreAb) is very scanty particularly in Nigeria.

Studies (Pomper, Wu and Snyder, 2003) have revealed that steady increase in the transmission of the disease is attributed to improper screening of the blood; also the virus can be transmitted by blood donors and organ donors who are positive for antibody to HBV core antigen (anti-HBc) but negative for all other HBV markers. This occult infection is one of the reasons for high risk of HBV infection. There may be possibility of missing out one marker when the other is negative among pregnant women posing a risk to their babies. The findings from this study will improve the management protocol of pregnant women when screened, hence the need for this study.

Scope of the Study

This study involved 350 pregnant women visiting three hospitals in Abuja for ante-natal care. Blood samples were collected from the pregnant women and screened for Hepatitis B virus using two serological markers (HBsAg and HBcoreAb). Methodology employed for the study includes collection of Demographic information and the screening of the blood samples using rapid HBV panel kit.

Aim and Objectives of the Study

This study was aimed at determining the prevalence of Hepatitis B among pregnant women visiting three hospitals in Abuja for ante-natal care with the following Objectives:

1. To screen blood samples for hepatitis B virus surface and core antibodies among pregnant women visiting the three hospitals for ante-natal care.
2. To determine the risk factors (age, history of surgery etc) associated with Hepatitis B virus infection among pregnant women in the study area.
3. To determine the relationship between HBsAg and HBcAb among pregnant women under investigation.

MATERIALS AND METHODS

Description of the study area

Abuja is the largest and the capital city of Nigeria, it has a human population close of 780,000 people. The city of Abuja is on latitude 9.0667°N and longitude 7.4833°E. The Territory is north of the confluence of the Niger and Benue Rivers. Abuja is bordered by Kaduna state to the north, Nassarawa state to the east, Kogi state to the south and Niger state to the west. It has land area of 2,824 square miles (7,315 square km). The average annual temperature is 27.2 °C in Abuja and about 1267 mm of precipitation falls annually. The occupation of the first inhabitants of Abuja (the Gbagyi) is farming, following the influx of people to Abuja the major occupation of the inhabitants are public servants and civil servants.

Sample size determination

The sample size for this research work was determined by the formula below

$$n = t^2 \times p(1-p)/m^2 \text{ (Aminu et al., 2009)}$$

Where,

n = required sample size

t = confidence level at 95%

p = prevalence rate of the disease

m = margin of error at 5%

Ethical Consideration

Ethical clearance was obtained from the research ethical committee of the Federal Capital Territory before blood samples collection

Sample collection

A total of 350 samples were collected using venipuncture from the pregnant women visiting the three hospitals (University of Abuja Teaching Hospital, National hospital and Zankli hospital) from July to December, 2014. A structured questionnaire was administered in order to obtain demographic information of the pregnant women before the collection of the samples. The breakdown of the blood samples collected from each of the three hospitals is as follows: University of Abuja Teaching Hospital -150, National Hospital - 50 and Zankli Hospital – 150. Five milliliter (5ml) of blood was taken from each of the 350 pregnant women recruited for the study. The blood samples were taken into EDTA bottles and transported to the serology laboratory of Zankli hospital for analysis

Sample preparation and screening

Blood samples were centrifuged separately at 1500 rpm for 5 minutes, plasma from each sample was aspirated and transferred into a sterile cryovial. The samples were stored at -20° C prior to screening. The frozen plasma was allowed to thaw before the tests devices were removed from the pouches, placed on a clean surface in the laboratory. The test devices were labeled with samples code for easy identification, three drops of specimens were dispensed into the sample wells using the sterile droppers and allowed to stand for 15 minutes. Readings were taken and recorded.

Quality Control of the Assay

A procedural control is incorporated in the device and is labelled "control". Control bar that did not turn red by assay completion was seen as invalid and was retested.

Interpretation of the test results

The test was said to be positive when red bands appeared in both the control and test region of the test device. When a red band appeared in the control region of the strip without any red band in the test (patient) region, the test was said to be negative. When no red band appeared in the control region, and when a red band appeared only in the test of the strip, these two tests were said to be invalid and the test was repeated to rule out errors

Statistical Analysis

Chisquare, student t- test was used to determine the level of significance between the considered factors and rate of infection.

RESULTS AND DISCUSSION

Results

Out of the 350 blood samples collected from pregnant women visiting three hospitals in Federal Capital Territory, Abuja, Nigeria, 34(9.7%) were found positive for hepatitis B virus surface antigen while 10(2.9%) were positive for hepatitis B virus core antibody.

Pregnant women within the age group 25-29 years recorded high prevalence of 3.7% for surface antigen while pregnant women within the age group 30-34 years had prevalence of 1.4% for hepatitis B virus core antibody (Table 1)

Table 1 Prevalence of hepatitis B virus surface antigen and core antibody

Age	HB surface Antigen			HB core Antibody		
	Sample screened	+ve	Prevalence (%)	Sample screened	+ve	Prevalence (%)
20-24	44	1	0.3	44	0	0
25-29	115	13	3.7	115	4	1.1
30-34	78	9	2.6	78	5	1.4
35-39	63	8	2.3	63	1	0.3

(t- test= 3.81, p<0.05, coefficient of correlation (r)= 0.900, coefficient of regression b=0.4)

Pregnant women with history of blood transfusion had prevalence of 2.3% surface antigen, 0.6% core antibody while those without history of blood transfusion had prevalence of 7.4% surface antigen and 2.3% core antibody (Table 2).

Table 2 Prevalence of HBV surface antigen and core antibody according to history of blood transfusion

Blood transfusion	HB surface Antigen			HB core Antibody		
	Sample screened	Positivity	Prevalence	Sample screened	Positivity	Prevalence
Yes	85	8	2.3	85	2	0.6
No	265	26	7.4	265	8	2.3
	350	34	9.7	350	10	2.9

(chisquare(X²)= 3.81, p>0.05, coefficient of correlation (r)= 0.997, coefficient of regression b=0.33)

Pregnant women with history of surgery and those without history of surgery recorded 4.86% each for HBV surface antigen. Similarly, pregnant women with and without history of surgery also had 1.43% each for hepatitis B virus core antibody (Table 3)

Table 3 Prevalence of HBV surface antigen and core antibody according to History of Surgery

History of surgery	HB surface Antigen			HB core Antibody		
	Sample screened	Positivity	Prevalence	Sample screened	Positivity	Prevalence
Yes	125	17	4.86	125	5	1.43
No	225	17	4.86	225	5	1.43
	350	34	9.7	350	10	2.9

(chisquare (X²)= 3.44, p>0.05, coefficient of correlation (r)= 1.000, coefficient of regression b=0)

Pregnant women that shared sharp objects had prevalence of 3.43% surface antigen, 1.14% core antibody while those without history of sharing sharps had prevalence of 6.29% surface antigen and 1.71% core antibody (Table 4).

Table 4 Prevalence of HBV surface antigen and core antibody according to lifestyle

Sharing of sharp objects	HB surface Antigen			HB core Antibody		
	Sample screened	Positivity	Prevalence	Sample screened	Positivity	Prevalence
Yes	102	12	3.43	102	4	1.14
No	248	22	6.29	248	6	1.71
	350	34	9.7	350	10	2.9

(chisquare (X²)= 1.07, p>0.05, coefficient of correlation (r)= 0.996, coefficient of regression b=0.2)

Pregnant women from polygamous homes had prevalence of 1.71% surface antigen and 0.29% had core antibody while those from monogamous homes recorded prevalence of 8% surface antigen and 2.57% core antibody (Table 5).

Table 5 Prevalence of HBV surface antigen and core antibody according to family type

Family type	HB surface Antigen			HB core Antibody		
	Sample screened	Positivity	Prevalence	Sample screened	Positivity	Prevalence
Polygamy	19	6	1.71	19	1	0.29
	331	28	8	331	9	2.7
Monogamy	350	34	9.7	350	10	2.9

(chisquare(X²)= 2.73, p>0.05, coefficient of correlation (r)= 0.995, coefficient of regression b=0.36)

Pregnant women who are non health workers had a prevalence of 8.57% surface antigen and 2.86% core antibody while prevalence of 1.14% surface antigen and 0% core antibody was recorded for those that are health workers (Table 6).

Table 6 Prevalence of HBV according to occupation of the pregnant women

Occupation	HB surface Antigen			HB core Antibody	
	Sample screened	Positivity	Prevalence	Positivity	Prevalence
Non health workers	318	30	8.57	10	2.86
Health workers	32	4	1.14	0	0.0
	350	34	9.7	10	2.9

(chisquare(X²)= 1.28, p>0.05, coefficient of correlation (r)= 0.991, coefficient of regression b=0.38)

Table 7 Relationship between the factors and the rate of infection

Factors	Positive samples	Positive samples	p-value
	<u>HBsurface</u>	core antibody	
Age(years)			
20-24	1	-	3.81
25-29	13	4	
30-34	9	5	
35-39	8	1	
40-44	3	-	
History of blood transfusion			
Yes	8	2	3.81
No	26	8	

History of surgery

Yes 17 5 3.44

No 17 5

Sharing sharp objects

Yes 12 4 1.07

No 22 6

Family type

Polygamous 6 1 2.73

Monogamous 28 9

Occupation

Non health workers 30 10 1.28

Health workers 4 -

Discussion

Transmission of hepatitis B virus (HBV) from mother to infant during the perinatal period is one of the most efficient modes of HBV infection which often leads to severe long-term diseases. In this study, prevalence of HBV surface antigen and core antibody among pregnant women visiting three hospitals in Abuja was determined to be 9.7% and 2.9% respectively. The high prevalence of HBsAg and HBcAb recorded in this study is comparable with the study conducted by Forbi, Onyemauwa, Gyar, Oyeleye, Entonu and Agwale (2008); Mbaawuaga, Enenebeaku, Okopi, Damen, (2008); Kuta *et al.*, (2014).

Pregnant women within the age group 25-29 years recorded prevalence of 3.7% for surface antigen while pregnant women within the age group 30-34 years had high prevalence of 1.4% for hepatitis B virus core antibody (Table 1). These findings agree with the report by Vazquez-Martinez *et al.*, (2003) and Olokoba *et al.*, (2011) who observed that the average age of women infected with the Hepatitis B virus was 26 years. The reason for the prevalence could be attributed to sexual activeness peculiar with women within the age group (25-29 years). Statistical analysis (Table 7) revealed that age of the pregnant women is a significant factor associated with the rate of infection.

Pregnant women with history of blood transfusion had prevalence of 2.3% surface antigen, 0.6% core antibody while those without history of blood transfusion had prevalence of 7.4% surface antigen and 2.3% core antibody (Table 2). Study by Ibrahim *et al.*, (2012) and Olokoba *et al.*, (2012) have reported similar incidences. Although the environment where the previous studies (Ibrahim *et al.*, 2012; Olokoba *et al.*, 2012) cannot be compared with the environment (Nigeria) where this study was conducted, the fact that similar procedures were used makes the outcome of this study comparable with the previous studies. Statistical analysis revealed that blood transfusion is not a factor in the infection rate with HBV (Table 7). Despite the revelation of the statistical analysis, the possibility of contracting HBV through blood transfusion is not in doubt.

Pregnant women with history of surgery and those without history of surgery recorded 4.86% each for HBV surface antigen. Similarly, pregnant women with and without history of surgery also had 1.43% each for hepatitis B virus core antibody (Table 3). Similar studies by Ibrahim *et al.* (2012) and Olokoba *et al.* (2012) have reported similar incidences among pregnant women with history of blood transfusion with a significant

relationship between the rate of infection and the factor (history of surgery). The result of this study is at variance with the previous studies (Table 7).

Pregnant women that share sharp objects had prevalence of 3.43% surface antigen, 1.14% core antibody while those without history of sharing sharp objects had prevalence of 6.29% surface antigen and 1.71% core antibody (Table 4). Similar study has been reported by Machado *et al.* (2013) with higher prevalence. The low prevalence recorded among pregnant women involved in this study could be attributed to good hygienic practices and awareness on the common routes of transmitting HBV. Chisquare analysis revealed that the use of sharp objects is not a significant factor.

Pregnant women from polygamous homes had prevalence of 1.71% surface antigen and 0.29% core antibody while those from monogamous homes recorded prevalence of 8% surface antigen and 2.57% core antibody (Table 5). This study corroborate the previous study by Frambo *et al.* (2014) but at variance with the report by Anaedobe, Fowotade, Omoruyi, Bakare, (2015). Chisquare analysis indicated no significant relationship between the rate of infection and the factor (polygamous or monogamous) considered (Table 7).

Pregnant women who are non health workers had a prevalence of 8.57% surface antigen and 2.86% core antibody while prevalence of 1.14% surface antigen only was recorded for those that are health workers (Table 6). Akani *et al.* (2005) has reported higher prevalence (17%) among public health workers. The low prevalence observed in this study could be attributed to awareness and war against the proliferation of untrained or half-baked medical personnels particularly in the rural settings. Despite the prevalence recorded among pregnant women that are health workers and non health workers, chisquare analysis revealed that working or not working in the health sector was not a factor in the transmission of HBV (Table 7).

CONCLUSION AND RECOMMENDATIONS

Conclusion

From the results of this study, the prevalence of Hepatitis B among pregnant women is high and reflects a high risk of Hepatitis B Virus perinatal transmission. The factors obtained from the demographic data of the pregnant women investigated revealed that there was no significant relationship between the rate of infection and

the factors considered. Indiscriminate blood transfusion by untrained medical personnel cannot be ruled out as a major contributing factor in the spread of the Hepatitis B virus infection. The study also observed less awareness about the disease (Hepatitis B) particularly the less privileged in the society.

Recommendations

Based on the results, it is recommended that all pregnant women be routinely screened for HBV with other markers because the use of other HBV infection serological markers such as anti HBs, anti HBcore (HB coreAb) and anti HBe will help to clearly differentiate a true negative person from a person having an occult HBV infection as well as providing information about the status of a pregnant woman. Community and hospital based studies should be encouraged to ascertain the true picture of the situation in FCT and the country at large. A strong surveillance strategy should be in place by government and private organizations to track the spread of the disease among many Nigerians.

Laura Madukaji- APIN Public Health Initiatives, Abuja, Nigeria

Ifeanyi Ossamulu- Federal University of Technology Minna, Niger, Nigeria

Grace Mambulla- Physician at Zankli Medical Centre, Abuja, Nigeria

Musa Galadima- Federal University of Technology Minna, Niger, Nigeria

Faruk Kuta- Federal University of Technology Minna, Niger, Nigeria

REFERENCES

Abbas, Z., Jafri, W., & Raza, S. (2010). Hepatitis D: Scenario in the Asia-Pacific region. *World Journal of Gastroenterology*, 16, 554-62.

Abiodun, P. O., & Omoike, I. U. (1990). Hepatitis B Surface Antigenemia in children in Benin City, *Nigerian Journal of Paediatrics*, 17, 27-31.

Aggarwal, R., Kini, D., Sofat, S., Naik, S., & Krawczynski, K. (2000). Duration of viremia and faecal viral excretion in acute hepatitis. *Lancet*, 356, 1081-1082

Ahizechukwu, C., Eke, I., Uzoamaka, A., Charles, O., Ifeanyi-chukwu, U., Ezebialu, B., & Chukwuanugo, O. (2011) Prevalence, correlates and pattern of hepatitis B surface antigen in a low resource setting *Virology Journal*, 4, 8-12

Akani, C.I., Ojule, A.C., Oporum, H.C., Ejilemele, A.A. (2005). Sero-prevalence of Hepatitis B surface antigen (HBsAg) in pregnant women in Port-Harcourt, Nigeria. *Nigeria Post-graduate Medical Journal*, 12(4), 266-270.

Akinbami, A.A., Oshinaike, O.O., Dosunmu, O.A., Adeyemo, T.A., Adediran, A., Akanmu, S., Wright, K.O.,... & Aile, K. (2012). Seroprevalence of hepatitis B e antigen (HBe antigen) and B core antibodies (IgG anti-HBcore and IgM anti-HBcore) among hepatitis B surface antigen positive blood donors at a Tertiary Centre in Nigeria. *BioMedical Central Research*, 5, 167-170.

Akriviadis, E., Botla, R., Briggs, W., Han, S., Reynolds, T., & Shakil, O. (2000). "Pentoxifylline improves short-term survival in severe acute alcoholic hepatitis: a double-blind, placebo-controlled trial". *Gastroenterology*, 119 (6), 1637-1648

Alavian, S.M., & Alavian, S.H. (2005). Hepatitis D virus infection; Iran, Middle East and Central Asia. *Hepatitis Monthly*, 5(4), 137-143.

Almeida, J.D., Rubenstein, D., & Stott, E.J. (1971). New antigen-antibody system in Australia-antigen positive hepatitis. *Lancet*, 10 (7736), 1225-1227

Aminu, M., Esona, M.D., Geya, A., and Steele, A.D. (2008). Epidemiology of Rotavirus and astrovirus infections in children in North-western Nigeria. *Annals of African Medicine*, 7(4), 168-174

Anaedobe, C.G., Fowotade, A., Omoruyi, C., Bakare, R. (2015) Prevalence, sociodemographic features and risk factors of Hepatitis B virus infection among pregnant women in Southwestern Nigeria. *The Pan African Medical Journal*, 20, 406

Ando, K., Guidotti, L., Wirth, S., Ishikawa, T., Missale, G., Moriyama, T., Schreiber, R., Schlicht, J., Huang, S., & Chisari, F. (1994). Class I-restricted cytotoxic T lymphocytes are directly cytopathic for their target cells in vivo. *Journal of Immunology*, 152, 3245-3253.

- Arankalle, V.A., Chobe, L.P., Joshi, M.V., Chadha, M.S., Kundu, B.S., & Walimbe, A.M. (2002) Human and swine hepatitis E viruses from Western India belong to different genotypes. *Journal of Hepatology*, 36, 417–425
- Ashbolt, N.J. (2004). Microbial contamination of drinking water and disease outcomes in developing regions. *Toxicology*, 198, 229–238
- Aspinall, E.J., Hawkins, G., Fraser, A., Hutchinson, S.J., & Goldberg, D. (2011). "Hepatitis B prevention, diagnosis, treatment and care: a review." *Occupational medicine (Oxford, England)*, 61 (8), 531–540.
- Barker, L.F., Shulman, N.R., Murray, R., Hirschman, R.J., Ratner, F., Diefenbach, W.C., & Geller, H.M. (1996). "Transmission of serum hepatitis". *Journal of the American Medical Association*, 276 (10), 841–844.
- Bartenschlager, R., Schaller, H. (1992) Hepadnaviral assembly is initiated by polymerase binding to the encapsidation signal in the viral RNA genome. *European Molecular Biology Organization Journal*, 11(9), 3413–3420
- Bartenschlager, R., Junker-Niepmann, M., & Schaller H. (1990). The P gene product of Hepatitis B Virus is required as a structural component for genomic RNA encapsidation. *Journal of Virology*, 64, 5324–5332
- Beasley, R.P., Trepo, C., Stevens, C.E., & Szmuness, W. (1997). The e antigen and vertical transmission of hepatitis B surface antigen. *American Journal of Epidemiology*, 105(2), 94–98.
- Beasley, R.P., Trepo, C., Stevens II, C.E. & Szmuness, W. (1977). "The e antigen and vertical transmission of hepatitis B surface antigen". *American Journal of Epidemiology*, volume 105, no. 2, pp 94–98.
- Beckel-Mitchener, A., & Summers, J. (1997) A novel transcriptional element in circular DNA monomers of the duck hepatitis B virus. *Journal of Virology*, 71, 7917–7922.
- Benn, J., & Schneider, R. (1994) Hepatitis B virus HBx protein activates Ras-GTP complex formation and establishes a Ras, Raf, MAP kinase signaling cascade. *Proceedings of National Academy of Science*, 91, 10350–10354
- Biron, C.A., Nguyen, K.B., Pien, G.C., Cousens, L.P., & Salazar-Mather, T.P. (1999) Natural killer cells in antiviral defense: function and regulation by innate cytokines. *Annual Review on Immunology*, 17, 189–220.
- Bloom, B.S., Hillman, A.L., Fendrick, A.M., & Schwartz, J.S., (1993). A reappraisal of hepatitis B virus vaccination strategies using cost-effectiveness analysis. *Annals of Internal Medicine*, 118, 298–306.
- Blumberg, B., & Alter, H. (1965). "A new" antigen in leukemia sera". *Journal of the American Medical Association*, 191, 101–106
- Bogdanos, D.P., Invernizzi, P., Mackay, I.R., & Vergani, D. (2008). "Autoimmune liver serology: Current diagnostic and clinical challenges". *World Journal of Gastroenterology*, 14 (21), 33774–3387
- Bruix, J., & Llovet, J.M. (2003) .Hepatitis B virus and hepatocellular carcinoma, *Journal of Hepatology*, 39(1), 59–63.
- Bruss, V. (2007). "Hepatitis B virus morphogenesis". *World Journal of Gastroenterology*, 13 (1), 65–73.
- Bruss, V., Hagelstein, J., Gerhardt, E., & Galle, P. R. (1996) .Myristylation of the large surface protein is required for hepatitis B virus in vitro infectivity. *Virology*, 218, 396–409
- Bruss, V., Lu, X., Thomssen, R., & Gerlich, W. (1994) Post-translational alterations in transmembrane topology of the hepatitis B virus large envelope protein. *European Molecular Biology Organization Journal*, 13, 2273–2279
- Buddeberg, F., Schimmer, B., Spahn, D. (2008). "Transfusion-transmissible infections and transfusion-related immunomodulation", Best

- Practice & Research. *Clinical Anaesthesiology*, 22 (3), 503–17.
- Center for Disease Control and Prevention. (2008). Recommendations for identification and public health management of persons with chronic hepatitis b virus infection. *Morbidity and Mortality Weekly Report*, 57(8), 9-11.
- Centers for Disease Control and Prevention (2010). Sexually transmitted diseases treatment guidelines. *Morbidity and Mortality Weekly Report*, 59(12), 1–110
- Centers for Disease Control and Prevention. (1998) Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. *Morbidity Mortality Weekly Report*, 47(19), 1-39.
- Centers for Disease Control and Prevention. (2008). Recommendations for identification and public health management of persons with chronic hepatitis C virus infection. *Morbidity and Mortality Weekly Report*, 57(RR-8), 1-20
- Chang, J., & Lewin, S. (2007). Immunopathogenesis of hepatitis B virus infection. *Immunology and Cell Biology*, 85,16-23.
- Chau, T.N., Lee, K.C, & Yao, H. (2004). "SARS-associated viral hepatitis caused by a novel coronavirus: report of three cases". *Hepatology*, 39 (2), 302–10
- Chen, H. S., Kaneko, S., Girones, R., Anderson, R. W., Hornbuckle, W. E., Tennant, B. C., Cote, P. J., Gerin, J. L., Purcell, R. H., & Miller, R. H. (1993). The woodchuck hepatitis virus X gene is important for establishment of virus infection in woodchucks. *Journal of Virology*, 67,1218–1226.
- Chen, M. T., Billaud, J.N., Sallberg, M.O., Guidotti, L.G., Chisari, F.V., Jones, J.I., ... & Milich, D.R. (2004). A function of the hepatitis B virus precore protein is to regulate the immune response to the core antigen. *Proceedings of the National Academy of Science USA* 101,14913-14918
- Cheng, A.L., Hsiung, C.A., Su, I.J., Chen, P.J., Chang, M.C., & Tsao, C.J. (2003). Lymphoma Committee of Taiwan Cooperative Oncology Group (TCOG). Steroid free chemotherapy decreases risk of hepatitis B virus (HBV) reactivation in HBV-carriers with lymphoma. *Hepatology*, 37,1320-1328.
- Chu, C.M., & Liaw, Y.F. (2004). Natural history differences in perinatally versus adult-acquired disease. *Current Hepatitis Reports* 3,123–131.
- Chu, C.M., & Liaw, Y.F. (2005). Genotype C hepatitis B virus infection is associated with a higher risk of reactivation of hepatitis B and progression to cirrhosis than genotype B: a longitudinal study of hepatitis B e antigen-positive patients with normal aminotransferase levels at baseline. *Journal of Hepatology*, 43,411–417.
- Chu, C.M., & Liaw, Y.F. (2007). HBsAg seroclearance in asymptomatic carriers of high endemic areas: appreciably high rates during a long-term follow-up. *Hepatology*, 45,1187–1192.
- Cindy, M., Weinbaum, M.D., Ian W., Eric, E., Mast, M.D., Susan, A., ... Ward, MD. (2008). Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection. *CDC Morbidity and Mortality Weekly Report*, 57(8), 1-20.
- Clements, C.J. (2006). Progress in the control of hepatitis B infection in the Western Pacific Region. *Vaccine*, 24,1975-1982.
- Comanor, L., Rifkin, O., Grigoriev, A., Minor, J., Kapke, G., & Kraiden, U. (1998). Assesment of HBV DNA stability in serum by Chiron Quantiplex assay. *Clinical Microbiology Journal*, 36(2), 382-386
- Cortez, H., Camilo, M., & Baptista, A. (1999). "Nonalcoholic fatty liver: another feature of the metabolic syndrome?" *Clinical Nutrition*, 18 (6), 353–358
- Cote, P. J., Toshkov, I., & Bellezza, C. (2000). Temporal pathogenesis of experimental neonatal woodchuck hepatitis virus infection: increased initial viral load and decreased severity of acute hepatitis during the development of chronic viral infection. *Hepatology*, 32, 807–817.

- Craxi, A., & Licata, A. (2006). Acute hepatitis C: In search of the optimal approach to cure. *Hepatology*, 43(2), 221–224.
- Curry, M., & Chopra, S. (2010). Acute viral hepatitis. In D. Mandell, J.E. Bennett, & R. Dolin (7th Edition), *Principles and practice of infectious diseases* (pp 1577-1592). Philadelphia, PA: Churchill Livingstone, Elsevier
- Dandri, M., & Locarnini, S. (2012). New insight in the pathobiology of hepatitis B virus infection. *Gut*, volume 61, no. Supplement 1, pp. i6-i17.
- Dane, D.S., Cameron, C.H., & Briggs, M. (1970). Virus-like particles in serum of patients with Australian antigen-associated hepatitis. *Lancet* 10 (7649), 695-698
- Dhédin, N., Douvin, C., & Kuentz, M. (1998). Reverse seroconversion of hepatitis B after allogeneic bone marrow transplantation: a retrospective study of 37 patients with pretransplant anti-HBs and anti-HBc. *Transplantation*, 66:616.
- Di Bisceglie, A.M. (2009). Hepatitis B and hepatocellular carcinoma. *Hepatology*, volume 49, no. Supplement5, pp. S56-S60
- Dickson, R.C., Everhart, J.E., Lake, J.R., Wei, Y.A., Seaberg, E.C., & Wiesner, R.H. (1997). NIDDK Liver Transplantation Database. Transmission of hepatitis B by transplantation of livers from donors positive for antibody to hepatitis B core antigen. *Gastroenterology*, 113,1668-1674.
- Dienstag, J.L. (1999). *Passive-active immunoprophylaxis after percutaneous exposure to hepatitis B virus*. *Hepatology*, 10,385-387.
- Dufour, D.R., Lott, J.A., Volte, F.S., Gretch, D.R., Koff, R.S., & Seeff, L.B.(2000). Diagnosis & Monitoring of hepatic injury in performance characteristic of Laboratory tests. *Clinical chemistry* 46(12), 2027-49
- Elena, S.F., Dopazo, J., Flores, R., Diener, T.O., Moya, A., Dopazo, F., & Diener, M. (1991). "Phylogeny of viroids, viroidlike satellite RNAs, and the viroidlike domain of hepatitis delta virus RNA". *Proceedings of the National Academy of Science*, 88 (13),5631–5634.
- Emechebe, G.O., Emodi, I.J., Ikefuna, A.N., Ilechukwu, G.C., Igwe, W.C., & Ejeofor, O.S.(2009). Hepatitis B virus infection in Nigeria- A review. *Nigeria Medical Journal*, 50(1),18-22
- Emerson, S.U., Anderson, D.A., Arankalle, A.V., Meng, X.J., Purdy, M.A., Schlauder, G.G., & Tsarev, S.A. (2004). Herpesvirus in Virus Taxonomy. *The Eighth Report of the International Committee on Taxonomy of Viruses*, 8, 851–855
- Ezegbudo, C. N., Agba, M. I., Agbonlahor, D. E., Nwobu, G O., Igwe, C. U., & Agba, M. I. (2004).The seroprevalence of hepatitis B Surface antigen and human immuno deficiency virus among pregnant women in Anambra state Nigeria. *Shiraz E-Medical Journal* , 5 , 20 - 22.
- Fairley, C.K., & Read, T.R. (2012). "Vaccination against sexually transmitted infections". *Current Opinion in Infectious Diseases* , 25 (1), 66–72.
- Fattovich, G., Giustina, G., & Sanchez-Tapias, J. (1998). Delayed clearance of serum HBsAg in compensated cirrhosis B: relation to interferon alpha therapy and disease prognosis. European Concerted Action on Viral Hepatitis (EUROHEP). *American Journal of Gastroenterology* 93,896–900.
- Fattovich, G. F., Bortolotti, F., & Francesco, D. (2008)."Natural history of chronic hepatitis B: Special emphasis on disease progression and prognostic factors", *Journal of Hepatology*, vol. 48, no. 2, pp. 335-352.
- Fong, T. L., Di Bisceglie, A. M., Biswas, R.A., Waggoner, J. G., Wilson, L.N., Claggett, J.U., & Hoofnagle, J. H. (1994). High levels of viral replication during acute hepatitis B infection predict progression to chronicity. *Journal of Medical Virology*, 43, 155–158**
- Forbi, J.C., Onyemauwa, N., Gyar, S.D., Oyeleye, A.O., Entonu, P., and Agwale, S.M. (2008). High prevalence of hepatitis B virus among female sex workers in Nigeria. *Revista do Instituto de Medicina Tropical de Sao Paulo*, 50(4), 219-221

- Fourel, G., Trepo, C., Bougueleret, L., Henglein, B., Ponzetto, A., Tiollais, P., & Buendia, M. A. (1990). Frequent activation of N-myc genes by hepadnavirus insertion in woodchuck liver tumours. *Nature*, 347, 294–298.
- Frambo, A.A., Atashili, J., Fon, P.N., & Ndumbe, P.M. (2014). Prevalence of HBsAg and knowledge about hepatitis B in pregnancy in the Buea Health District, Cameroon: a cross-sectional study. *BioMedCentral Research Notes*, 7, 394. doi:10.1186/1756-0500-7-394
- Franzese, O., Kennedy, P., Gehring, A., Gotto, J., Williams, R., Maini, M., & Bertoletti, A.** (2005). *Modulation of the CD8⁺-T-cell response by CD4⁺ CD25⁺ regulatory T cells in patients with hepatitis B virus infection.* *Journal of Virology* 79, 3322– 3328
- Gallegos-Orozco, J.F., & Rakela-Brödner, J. (2010). "Hepatitis viruses: not always what it seems to be". *Revista Medica de Chile*, 138, (10), 1302–1311.
- Ganem, D., Pollack, J., & Tavis, J. (1994). Hepatitis B virus reverse transcriptase and its many roles in hepadnaviral genomic replication. *Infectious Agents and Disease* 3, 85–93.
- Ganem, D. (1996). Hepadnaviridae and their Replication. In B. N. Fields, D. M. Knipe, P. M. Howled. 3rd edition, *Fundamental Virology* (pp.490-502). Philadelphia: Lippincott-Raven Publishers
- Gerin JL, Casey JL, Bergmann KF. The molecular biology of hepatitis delta virus: recent advances. In K. Nishoka, H. Suzuki, S. Mishiro, T. Oda (eds), *Viral hepatitis and liver disease* (pp 380-441) Tokyo, Springer-Verlag
- Ghabril, M., Chalasani, N., & Björnsson, E. (2010). "Drug-induced liver injury: a clinical update". *Current Opinion in Gastroenterology*, 26 (3), 222–226
- Guidotti, L., Matzke, B., Schaller, H., & Chisari, F. (1995) High-level hepatitis B virus replication in transgenic mice. *Journal of Virology*, 69, 6158–6169
- Guidotti, L. G., & Chisari, F. V. (2001). Noncytolytic control of viral infections by the innate and adaptive immune response. *Annual Review on Immunology*, 19, 65–69.
- Habiba, S.A., Memon, M.A. (2007). Prevalence of Hepatitis B infection in pregnant women in a tertiary care hospital. *Infectious Disease Journal of Pakistan*, 4(7), 35-38.
- Hadziyannis, S.J. (2011), Natural history of chronic hepatitis B in Euro Mediterranean and African Countries. *Journal of Hepatology*, 55(1), 183-191.
- Hagan, H., Pouget, E., & Des Jarlais, D. (2011). A systematic review and meta-analysis of interventions to prevent hepatitis C virus infection in people who inject drugs. *The Journal of infectious diseases*, 204 (1), 74–83.
- Harrison, T. J., Dusheiko, G. M., & Zuckerman, A. J. (2009). Hepatitis Viruses. In A. J. Zuckerman, J. E. Banatvala, B. D. Schoub, P. D. Griffiths & P. Mortimer (6th Edition), *Principles and Practice of Clinical Virology* (pp.1112-1120). Chichester, UK, John Wiley & Sons, Ltd
- Hauri, A.M., Armstrong, G.L., & Hutin, Y.J. (2004). The global burden of disease attributable to contaminated injections given in health care settings. *International Journal of STD & AIDS*, 15, 7–16.
- Hilleman, M.R. (2003). Critical overview and outlook: pathogenesis, prevention, and treatment of hepatitis and hepatocarcinoma caused by hepatitis B virus. *Vaccine*, 21(32), 4626-4649.
- Hirschman, S.Z., Vernace, S.J., & Schaffner, F. (1971). DNA polymerase in preparations containing Australia antigen. *Lancet*, 10 (7709), 1099-1103
- Hollinger, F.B., Liang, T.J. (2001). Hepatitis B Virus. In D.M. Knipe (4th Edition), *Fields Virology* (pp 2971-3036). Philadelphia, Lippincott Williams & Wilkins.
- Hollinger, F.B., Habibollahi, P., Daneshmand, A., & Alavian, S.M. (2010) "Occult hepatitis B infection in chronic hemodialysis patients: Current concepts and strategy". *Hepatitis Monthly*, vol. 10, no. 3, pp. 199-204.
- Hoofnagle, J.H. (1991). Type B Hepatitis, *Virology, serology and clinical course.* *Seminars in liver disease*, 11,73-83

- Hoofnagle, J.H., & Bisceglie, A.M. (1991). Serologic diagnosis of acute and chronic viral hepatitis. *Seminars in Liver disease* 11(2), 73-83
- Hsu, Y.S., Chien, R.N., & Yeh, C.T. (2002) Long-term outcome after spontaneous HBeAg seroconversion in patients with chronic hepatitis B. *Hepatology*,35,1522–1527.
- Hung, S.J., Lin, J.G., Tai, D.I., Liaw, Y.F., & Chu, C.M.(2004) .Natural history of hepatitis B e antigen to antibody seroconversion in patients with normal serum aminotransferase levels. *American Journal of Medicine* 116,829–834.
- Huo, T.I., Wu, J.C., & Lee, P.C. (1998). Sero-clearance of hepatitis B surface antigen in chronic carriers does not necessarily imply a good prognosis. *Hepatology*, 28,231–236.
- Hwang, L., Lee, G., & Beasley, R. (1999). *Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. Lancet I*, 1099-1102.
- Hyams, K.C. (1995). Risks of chronicity following acute hepatitis B virus infection: a review. *Clinical Infectious Disease*, 20(4),992-1000.
- Ibrahim, B., Mohamed, S., Mahfouz, S., Erwa, M., Abdelrahim, G., Ibrahim,...Ageely, M. (2012). Prevalence and Risk Factors of Hepatitis B Virus among Pregnant women in Jazan Region-Kingdom of Saudi Arabia. *Journal of Biology, Agriculture and Healthcare*, 2(8),45-48
- Imade, G.E., Sagay, A.S., Ugwu, B.T., Thatcher, T.D., Ford, R.W.(2004). Sero-prevalence of Hepatitis B and Human Immunodeficiency Virus infections in pregnant women in Nigeria.*Journal of Medicine in the Tropics*, 6(2),15-21.
- Ivlustapha, S. K., & Jibrin, Y. B. (2004). The Prevalence of Hepatitis B Surface Antigenemia in Patients with Human Immunodeficiency Virus infection in Gombe, Nigeria. *Annual African Medical Journal*, 4, 10-14.
- Jang, I.W., Choi, I.Y., & Bae, S.H. (2004). Transarterial chemo-lipiodolization can reactivate hepatitis B virus replication in patients with hepatocellular carcinoma. *Journal of Hepatology*, 41,427.
- Janssen, H.L., van Zonneveld, M., Senturk, H., Zeuzem, S., Akarca, U.S., & Cakaloglu, Y.(2005). Pegylated interferon alfa-2b alone or in combination with lamivudine for HBeAg-positive chronic hepatitis B: a randomized trial. *Lancet*, 365, 123-129.
- Julian, D., & Dorathy, D. (2010). Origin and evolution of antibiotic resistance. *Molecular Microbiology*,74,(3),417-433
- Jun, Z., Shao-Wei, L., Ting, W., Qinjian, Z., Mun-Hon, N., Ning-Shao, X. (2012). Hepatitis E virus: neutralizing sites, diagnosis, and protective immunity. *Reviews in Medical Virology*, 22, 339–349
- Kakimi, K., Guidotti, L., Koezuka, Y., & Chisari, F. V. (2000). Natural killer T cell activation inhibits hepatitis B virus replication in vivo. *Journal of Experimental Medicine* ,192, 921–930
- Kay, A., and Zoulim, F. (2007). "Hepatitis B virus genetic variability and evolution". *Virus Research*, 127 (2), 164–176
- Kim, Y., Choi, M., Park, Y., Kim, S., Lee, M., & Jung, U. (2013). Garcinia Cambogia attenuates diet-induced adiposity but exacerbates hepatic collagen accumulation and inflammation. *World Journal of Gastroenterology*, 9(29), 4689-4701.
- Korenman, J., Baker, B., & Waggoner, J. (1991). Long-term remission of chronic hepatitis B after alpha-interferon therapy. *Annals of Internal Medicine*, 114,629-634.
- Kraiden, M., Minor, J., Rifke, O., & Comanor, L. (1999). Effect of multiple freeze- thaw cycle on HBV DNA. *Clinical Microbiology Journal* 37, 1683-1686
- Krawczynski, K., Mast, E., & Perdy, M. (1997).Hepatitis E : an overview. In M. Rizzetto, R. Purcell, J. Gerin and G. Verme (Eds). *Viral hepatitis and liver disease, Turin, Mineroa Medica*, (pp. 305-312)
- Krawitt, E. L. (1996). Autoimmune hepatitis. *New England Journal of Medicine*, 334 (14), 897–903.

- Krishnan, M., Worden, J., & Hardwick, U. (2008). Recovery of diverse genes for class I integron-integrases from environmental DNA samples *FEMS Microbiology*, 287,56-62
- Kuta, F.A., Wakaso, I., and Adamu, A. (2014). Seroprevalence of Hepatitis B virus surface antigen infection among pregnant women visiting for ante-natal care. *Journal of Medical and Applied Biosciences*, 2(1), 48-51. Retrieved from: <http://www.irjset.com>
- Lai, C.L., Chien, R.N., Leung, N.W., Chang, T.T., Guan, R., Tai, DII. (1998). One-year trial of lamivudine for chronic hepatitis B. Asia Hepatitis Lamivudine Study Group. *New England Journal of Medicine* 339, 61-68.
- Lampertico, P., Ninno, E., Vigano, M., Romeo, R., Donato, M., Sablon, E. (2003). Long-term suppression of hepatitis B e antigen-negative chronic hepatitis B by 24-month interferon therapy. *Hepatology*, 37,756-763.
- Lau, G.K., Leung, Y.H., Fong, D.Y. (2002). High hepatitis B virus (HBV) DNA viral load as the most important risk factor for HBV reactivation in patients positive for HBV surface antigen undergoing autologous hematopoietic cell transplantation. *Blood*, 99, 2324.
- Lau, G.K. (2008). Hepatitis B reactivation after chemotherapy: two decades of clinical research. *Hepatology* 2,152-162.
- Lavanchy, D. (2004) Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *Journal of Viral Hepatitis* 11, 97-107.
- Lee, P.I., Lee, C.Y., Huang, L.M., Chen, J. M., & Chang, M. H. (1995). A follow-up study of combined vaccination with plasma-derived and recombinant hepatitis B vaccines in infants. *Vaccine*, volume 13, no. 17, pp. 1685-1689.
- Lee, S.D., Lo, K.J., Tsai, Y.T., Wu, J.C., Wu, T.C., Yang, Z.L., Ng, H.T. (1998). The role of cesarean section in the prevention of mother-infant transmission of hepatitis B virus. *Lancet*. 2, 833-37
- Lee, W.M. (1997). Hepatitis B virus infection. *New England Medical journal*. 11, 337, 1733-1745.
- Leung, N. (2009). Chronic hepatitis B in Asian women of childbearing age. *Hepatology International*, vol. 3, supplement 1, pp. 24-31
- Lew, Y.Y., & Michalak, T. I. (2001). In vitro and in vivo infectivity and pathogenicity of the lymphoid cell-derived woodchuck hepatitis virus. *Journal of Virology* 75, 1770-1782.
- Liaw, Y.F., Sheen, I.S., Chen, T.J., Chu, C.M., & Pao, C.C.(1991). Incidence, determinants and significance of delayed clearance of serum HBsAg in chronic hepatitis B virus infection: a prospective study. *Hepatology*, 1,627-631.
- Linnen, J., Wages, J., & Zhang-Keck, Z.Y. (1996). "Molecular cloning and disease association of hepatitis G virus: a transfusion-transmissible agent". *Science* ,271 (5248), 505-8.
- Lo, K., Wu, J., & Lee, S. (1996). *Prevention of maternal-infant hepatitis B virus transmission by immunization: the role of serum hepatitis B virus DNA*. *Hepatology* 6:369-373.
- Locarnini, S. (2004) Molecular virology of hepatitis B virus. *Seminar in Liver Diseases*, 24,3-10.
- Lok, A.S., & McMahon, B.J. (2009) "Chronic Hepatitis B: Update 2009". *Hepatology*, volume 50, no. 3, pp. 1-36.
- Loomba, R., Rowley, A., Wesley, R., Liang, T., Hoofnagle, J., & Pucino, F. (2008). Systematic review: the effect of preventive lamivudine on hepatitis B reactivation during chemotherapy. *Annals of Internal Medicine* , 148,519-528.
- Lozano, R., Naghavi, M., & Foreman, K. (2010). 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. *The Lancet*, 380, 2095-2128.
- Luka, S.A., Ibrahim, M.B., Iliya, S.N.(2008). Sero-prevalence of Hepatitis B surface antigen among pregnant women attending Ahmadu Bello

- University Teaching Hospital, Zaria, Nigeria. *Nigerian Journal of Parasitology*, 29(1),38-41
- Lund, J., Sato, A., Akira, S., Medzhitov, R., & Iwasaki, A. (2003). Toll-like receptor 9-mediated recognition of herpes simplex virus-2 by plasmacytoid dendritic cells. *Journal of Experimental Medicine*, 198, 513–520.
- Lurmann, A. (1885). "Eine icterus epidemic". *Berl Klin Wochenschr* (in German) 22,20–23.
- Machado, D.F., Martins, T., Trevisol, D.J., Vieira e Silva, R.A., Narciso-Schiavon, J.L., Schuelter-Trevisol, F.(2013) Prevalence and Factors Associated with Hepatitis B Virus Infection among Senior Citizens in a Southern Brazilian City. *Hepatitis Monthly*,13(5),e7874.DOI: .5812/hepatmon.7874
- Magnius, L., & Norder, H. (1995). Subtypes, genotypes and molecular epidemiology of the hepatitis B virus as reflected by sequence variability of the S-gene. *Intervirology* ,38 (1–2), 24-34.
- Mahoney, F.J. (1999). Update on diagnosis, management and prevention of hepatitis B virus infection. *Clinical microbiology review* 12,351-366
- Mahoney, F., & Kane, M. (1999). Hepatitis B vaccine. In S.A. Plotkin & W.A. Orenstein(Eds.), *Vaccines* (pp158-182). 3rd ed. Philadelphia, W.B. Saunders Press
- Malaguarnera, G., Cataudella, E., Giordano, M., Nunnari, G., Chisari, G., Malaguarnera, M. (2012). Toxic hepatitis in occupational exposure to solvents. *World Journal of Gastroenterology*, 18 (22), 2756–2866.
- Manns, M.P., & Strassburg, C.P. (2011). Therapeutic strategies for autoimmune hepatitis. *Digestive diseases*, 29, (4), 411–415
- Marcellin, P., Lau, G., Bonino, F., Farci, P., Hadziyannis, S., & Jin, R. (2004). Peginterferon alfa-2a alone, lamivudine alone, and the two in combination in patients with HBeAg-negative chronic hepatitis B. *New England Journal of Medicine*, 351,1206-1217.
- Marchesini, G., Brizi, M., & Bianchi, G.(2001). "Nonalcoholic fatty liver disease: a feature of the metabolic syndrome". *Diabete*, 50 (8), 1844–1850..
- Markowitz, J.S. (1998). Prophylaxis against hepatitis B recurrence following liver transplantation using combination lamivudine and hepatitis B immune globulin. *Hepatology*, 28,585-589.
- Mast, E.E., Weinbaum, C.M, & Fiore, A.E. (2006). A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. *Morbidity and Mortality Weekly Report*, 8,55(RR-16),1-33.
- Masuoka, C., Howard C., & Chalasani, N. (2013). "Nonalcoholic fatty liver disease: an emerging threat to obese and diabetic individuals". *Annals of the New York Academy of Sciences*,1281 (1), 106–122.
- Maurer, J., Hofacre, C and Summers, A (2004) Gram-positive bacteria are a major reservoir of class I antibiotic resistance integrons in poultry litter. *Academic Science Journal* 106,1061-1065
- Mbaawuaga, E.M., Enenebeaku, M.N.O., Okopi, J.A., Damen, J.G.(2008). Hepatitis B virus infection (HBV) among pregnant women in Makurdi, Nigeria. *African Journal of Biomedical Research* , 11,155-159.
- Mbaawuaga, E.M., Iroegbu, C.U. & Ike, A.C. (2014). Hepatitis B Virus (HBV) Serological Patterns in Benue State, Nigeria. *Open Journal of Medical Microbiology*, 4, 1-10. <http://dx.doi.org/10.4236/ojmm.2014.41001>
- McCullough AJ, O'Connor JF (1998). "Alcoholic liver disease: proposed recommendations for the American College of Gastroenterology". *American Journal of Gastroenterology*, 93 (11), 2022–36.
- McKenzie R, Fried MR, Sallie R.(1995) Hepatic failure and lactic acidosis due to fialuridine (FIAU), an investigational nucleoside analogue for chronic

- hepatitis B. *New England Journal of Medicine* ,333,1099-1105.
- Melnick, J.L.(1996). Properties and classification of hepatitis A virus. *Vaccine*, 10(1), 24–S26
- Mohammad, A., Riyasat, A., Luqman, A., Husain, S.A.,Rajiv, S., & Kar, R.(2010) Significance of anti-HBc screening of blood donors & its association with occult hepatitis B virus infection: Implications for blood transfusion. *Indian Journal Medical Research* 132, 312-317
- Moretta, L., Bottino, C., Pende, D., Vitale, M., Mingari, M. C., & Moretta, A.** (2005). *Human natural killer cells: molecular mechanisms controlling NK cell activation and tumor cell lysis*. *Immunology Journal*, 100, 7–13
- Multimer, D. J., Olomi, A., Skidmore, S., Olomu, N., Ratcliffe, D., Rodger, S. (1994).Viral hepatitis in Nigeria-sickle cell disease and commercial blood donors. *African Journal of Biomedical Research* , 87: 407-411.
- Nagao, Y., Matsuoka, H., Kawaguchi, T., Ide, T., Sata, M. (2008). HBV and HCV infection in Japanese dental care workers. *International Journal of Molecular Medicine* 21(6), 791-799
- Naides SJ (1998). "Rheumatic manifestations of parvovirus B19 infection". *Rheumatic Disease. Clinical North American Journal*. 24 (2): 375–401.
- Nakamoto, Y., Kaneko, S., & Cuevas, A.(2003). "Mechanisms of viral hepatitis induced liver injury". *Current Molecular Medicine*. 3 (6), 537–44.
- Naoumov, N.V., & Eddleston, A.L. (1994). Host immune response and variations in the virus genome: pathogenesis of liver damage caused by hepatitis B virus. *British Medical Journal* 35(8), 1013–1017.
- Navarro, D., Victor, J., Semone, B., John, R. (2006). Drug-Related Hepatotoxicity. *New England Journal of Medicine* 354 (7), 731–739.
- Navascues, C.A., Rodriguez, M., & Sotorrio, N.G. (1995). Epidemiology of hepatitis D virus infection: changes in the last 14 years. *American Journal of Gastroenterology*, 90, 1981-1984.
- Nelson, J.F., Frederick, L.M., Torimiro, J.N., Nana, P.N., Koh, M.V., & Takang, W.(2013). Prevalence, correlates and pattern of Hepatitis B among antenatal clinic attenders in Yaounde-Cameroon: is perinatal transmission of HBV neglected in Cameroon? *BMC Pregnancy and Childbirth* 13,158 doi: 10.1186/1471-2393-13-158
- Nguyen, N.H., & Keeffe, E.B. (2002). Screening for hepatocellular carcinoma. *Journal of Clinical Gastroenterology*, 35, 86-91
- Niederau, C., Heintges, T., & Lange, S. (1996). Long-term follow-up of HBeAg-positive patients treated with interferon alfa for chronic hepatitis B. *New England Journal of Medicine* 334,1422–1427.
- Niro, G., Ciancio, A., Gaeta, G., Smedile, A., Marrone, A., & Olivero, A. (2006). Pegylated interferon alpha-2b as monotherapy or in combination with ribavirin in chronic hepatitis delta. *Hepatology*. 44, 713-720.
- Nobili, V., Marcellini, M.,& Devito, R. (2006). "NAFLD in children: A prospective clinical-pathological study and effect of lifestyle advice". *Hepatology*. 44 (2), 458–465.
- Norman, G. (1997). Hepatitis B: diagnosis, prevention, and treatment. *Clinical Chemistry*, volume 43,8, 1500-1506
- Obi, R.K., Umeh, S.C., Okurede, O.H., Iroagba, I.I.(2006). Prevalence of hepatitis B virus infection among pregnant women in an antenatal clinic in Port Harcourt, Nigeria *African Journal of Clinical Experimental Microbiology*,7,78-82.
- Okano, M., Gallegos-Orozco, J., Rakela-Brödner, J., & Gross, T.(2010). "Hepatitis viruses: not always what it seems to be". *Nigerian Medical journal*, 138 (10), 1302–1311.
- Okano, M., & Gross, T. (2011). Acute or Chronic Life-Threatening Diseases Associated With Epstein-Barr Virus Infection. *American Journal of Medical Science*, 343 (6), 483–489.
- Okonko I., Okerentugba, P., Innocent-Adiele, H.(2012). Detection Of Hepatitis B Surface Antigen

- (HBsAg) Among Children In Ibadan, Southwestern Nigeria. *The Internet Journal of Infectious Diseases*, 10, 1
<http://www.biomedcentral.com/1756-0500/7/394>
- Olokoba, A.B., Salawu, F.K., Danburam, A., Olokoba, L.B., Midala, J.K., Badung, L.H., Awo, O. (2011). Hepatitis B virus infection amongst pregnant women in North-Eastern Nigeria- A call for action. *Nigerian Journal of Clinical Practice*, 14(1), 10-13
- Oluwatoyin, J.M., Olufisayo, A.A., Donbraye, E.I., & Adewumi, M.O. (2011). Hepatitis B Core IgM antibody (anti-HBcIgM) among hepatitis B Surface antigen (HBsAg) negative blood donors in Nigeria. *Virology Journal*, 8, 513, doi: 10.1186/1743-422X-8-513
- Onozawa, M., Hashino, S., Izumiyama, K., Kahata, K., Chuma, M., Mori, A. (2005). Progressive disappearance of anti-hepatitis B surface antigen antibody and reverse seroconversion after allogeneic hematopoietic stem cell transplantation in patients with previous hepatitis B virus infection. *Transplantation*, 79, 616-619.
- Onwuakor, C.E., Eze, V.C., Nwankwo, I.U., Iwu, J.O. (2014). "Sero-prevalence of Hepatitis B Surface Antigen (HBsAg) amongst Pregnant Women Attending Antenatal Clinic at the Federal Medical Centre Umuahia, Abia State, Nigeria." *American Journal of Public Health Research*, 2.6 (2014), 255-259.
- Pagano, G., Pacini, G., & Musso, G. (2002). "Nonalcoholic steatohepatitis, insulin resistance, and metabolic syndrome: further evidence for an etiologic association". *Hepatology*, 362 (35), 367-372.
- Pak, E., Esrason, K., & Wu, V. (2004). "Hepatotoxicity of herbal remedies: an emerging dilemma". *Progress in transplantation* 14 (2), 91-106.
- Patel, M., Emerman, M., & Malik, H. (2011). **Paleovirology - ghosts and gifts of viruses past**, *Current Opinion in Virology*, 1 (4), 304-309.
- Pawlotsky, J.M. (2002). Molecular diagnosis of viral hepatitis. *Gastroenterology* 122, 1554-1568
- Poland, G.A., & Jacobson, R.M. (2004). Clinical practice: prevention of hepatitis B with the hepatitis B vaccine. *New England Journal of Medicine* 351, 2832-2838.
- Pomper, G.J., Wu, Y., Snyder, E.L. (2003). Risks of transfusion-transmitted infections. *Current Opinion in Hematology* 10(6), 412-441
- Previsani, N., & Lavanchy, D. (2002) World Health Organization. Hepatitis B (WHO/CDS/CSR/LYO/2002.2). Available on: http://www.who.int/csr/disease/hepatitis/HepatitisB_who_cds_csr_lyo_2002_2.pdf [Accessed on: 24 August 2012]
- Prince, A., & Ganem, D. (2004), Hepatitis B Virus infection, natural history and clinical consequences. *New England Journal of Medicine* 350, 1118-1129
- Qinjian, Z., Jun, Z., Ting, W., Shao, W., Mun-Hon, N., Ning-Shao, X., & Wai-Kuo Shih, J. (2013) Antigenic determinants of hepatitis E virus and vaccine-induced immunogenicity and efficacy. *Journal of Gastroenterology*, 48, 159-168.
- Raimondo, G., Pollicino, T., Cacciola, I., & Squadrito, G. (2007). Occult hepatitis B virus infection. *Journal of Hepatology*, volume 46, no. 1, pp. 160-170.
- Raj, S., Stephen, T., & Debski, R. (2011). "Giant Cell Hepatitis With Autoimmune Hemolytic Anemia: A Case Report and Review of Pediatric Literature". *Clinical Pediatrics* 50 (4), 357-359
- Rehermann, B. (2003). Immune responses in hepatitis B virus infection. *Seminars in liver disease* 23, 21-38
- Rehermann, B., Ferrar, i C., Pasquinelli, C., & Chisari, F. (1996) Hepatitis B virus persists for decades after patient's recovery from acute viral hepatitis despite active maintenance of a cytotoxic T-lymphocyte response. *Nature Medicine* 2, 1104-1108
- Robinson, W.S., Clayton, D.A., Greenman, R.L. (1974) DNA of human hepatitis B virus candidate. *Journal virology*, 10, 384-391
- Roingard, P., Diouf, A., Sankale, J.L., Boye, C., Mboup, S., Diadhiou, F. (1993). Perinatal transmission of

- hepatitis B virus infection in Senegal, West Africa. *Viral Immunology*, 6, 65-73.
- Rosman, A., Waraich, A., Galvin, K., Casiano, J., Paronetto, F., & Lieber, C. (1996). "Alcoholism is associated with hepatitis C but not hepatitis B in an urban population". *The American journal of gastroenterology*, 91 (3), 498-505.
- Ryder, S., & Beckingham, I. (2001). "Acute hepatitis". *British Medical Journal*, 322 (7279), 151-153.
- Sadakazu, U., Hiroaki, O., Hiroko, I., Kiyoshi, B., Fumio, T., Yuzo, M., & Makoto, M. (1999). Serological detection of hepatitis B Virus genotypes by ELISA. *Journal of Virological Methods*, volumes 80,1,97-112
- Santos, J.K., Choquette, M., & Bezerra, J.A. (2010). "Cholestatic liver disease in children". *Journal of Gastroenterology*, 12 (1), 30-39.
- Sarich, T.C., Adams, S.P., Petricca, G.I., & Wright, J.M. (1999). "Inhibition of isoniazid-induced hepatotoxicity in rabbits by pretreatment with an amidase inhibitor". *Journal of Pharmacology*, 289 (2), 695-702.
- Schädler, S., & Hildt, E. (2009). HBV Life Cycle: Entry and Morphogenesis. *Viruses*, 1(2), 185-209.
- Schalm, S.W., Heathcote, J., Cianciara, J., Farrell, G., Sherman, M., & Willems, B. (2000). Lamivudine and alpha interferon combination treatment of patients with chronic hepatitis B infection: a randomised trial. *Gut* 46,562-568.
- Seyed Reza, M., Azar, S., Kouros, C., Mohammad, R. N., Hamid, M.S., & Mohammad, R.Z. (2011). Hepatitis C and Hepatitis B Virus Infection: Epidemiology and Risk Factors in a Large Cohort of Pregnant Women in Lorestan, West of Iran. *Hepatology Monthly*, 11(9), 736-739
- Siebert, D. (1998). Hepatitis B; issues in laboratory diagnosis and vaccination. *Australian Journal of Infectious diseases*, 21,72-75
- Song, Y., Sung, J., Yang, S., Choe, Y., Chang, Y., & Park, W. (2007). Factors associated with immunoprophylaxis failure against vertical transmission of hepatitis B virus. *European Journal of Pediatrics*, volume 166, no. 8, pp. 813-818.
- Subrat, K.P., & Satya, P.K. (2013). Epidemiology, Experimental Models, and Prevention: Zoonotic Aspects of Hepatitis E. *Viral Hepatitis*, 2, 431-441
- Sureau, C. (2006). The role of the HBV envelope proteins in the HDV replication cycle. *Current Topics in Microbiology and Immunology* 307, 113-31
- Taghavi, S.A., Sedighi, S., Mehrabani, D., Khademolhosseini, F. (2008). Hepatitis D in chronic active hepatitis B: prevalence, liver enzyme levels and histopathology- an epidemiological study in Shiraz, southern Iran, 2003-2004. *Hepatitis Monthly*, 8, 248-251.
- Tai, D.I., Lin, S.M., Sheen, I.S., Chu, C.M., Lin, D.Y., Liaw, Y.F. (2009). Long term outcome of hepatitis B e antigen-negative hepatitis B surface antigen carriers in relation to changes of alanine aminotransferase levels over time. *Hepatology*, 49,1859-1867.
- Tedder, R., Iyaz, S., Gilbert, N., Barbara, J., Corden, S., Gilson, R., & Boxall, E. (2002) Evidence for a dynamic host-parasite relationship in e-negative hepatitis B carriers. *Journal of Medical virology* 68,505-12
- ter Borg, M.J., Leemans, W.F., de Man, R.A., Janssen, H.L. (2008). Exacerbation of chronic hepatitis B infection after delivery. *Journal of Viral Hepatitis*, 15,37-41.
- Terrault, N.A. (2013). Sexual transmission of hepatitis C virus among monogamous heterosexual couples: The HCV Partners Study. *Hepatology*, 57(3), 881-889.
- Teuber, G., Dienes, H., Meyer, Z., Büschenfelde, K., & Gerken, G. (1996) Long-term follow-up of patients with chronic hepatitis B after interferon treatment. *Gastroenterology*, 34,230-236.
- Teufel, A., Galle, P., & Kanzler, S. (2009). "Update on autoimmune hepatitis". *World Journal of Gastroenterology* 15 (9), 1035-1041

- Thimme, R., Wieland, S., Steiger, C., Ghayeb, J., Reimann, K., Purcell, R., & Chisari, F. (2003). CD8⁺ T cells mediate viral clearance and disease pathogenesis during acute hepatitis B virus infection. *Journal of Virology* 77, 68–76.
- Tong, M.J., Nguyen, M.O., Tong, L.T., Blatt, L. (2009). Development of hepatocellular carcinoma after seroclearance of hepatitis B surface antigen. *Clinical Gastroenterology Hepatology*, 7,889–893.
- Unke, C.J., Ogbu, O., Inyama, P.U., Anyanwu, G.I., Njoku, M.O., Idoko, J.H.(2005). Prevalence of hepatitis-B surface antigen among blood donors and human immunodeficiency virus-infected patients in Jos, Nigeria. *Mem Inst Oswaldo Cruz*,100,13-6.
- Vartanian, J., Pineau, P., Henry, M., Hamilton, W., Muller, M. (2002). Identification of a hepatitis B virus genome in wild chimpanzees (*Pan troglodytes schweinfurthi*) from East Africa indicates a wide geographical dispersion among equatorial african primates. *Journal of Virology* 76, 11155–11158.
- Vazquez-Martinez, J., Coreno-Juarez, M.O., Montano-Estrada, L.F., Michael, A., Gomez-Dantez, H. (2003) Sero-prevalence of Hepatitis B in pregnant women in Mexico. *Salud Pública De México*, 45(3),165-170..
- Velu, V., Saravanan, S., Nandakumar, S., Dhevahi, E., Shankar, E., Murugavel, K., Kumarasamy, T., & Thyagarajan, S. (2008).Transmission of "a" determinant variants of hepatitis B virus in immunized babies born to HBsAg carrier mothers. *Japanese Journal of Infectious Disease*, 61(1), 73-6.
- Walsh, T.R (2006). Combinational genetic evolution of multi resistance; Current opinion. *Microbiology Journal*, 9,476-482
- Webster, G. J., Reignat, S., & Maini, M. K. (2000). Incubation phase of acute hepatitis B in man: dynamic of cellular immune mechanisms. *Hepatology*, 32, 1117–1124.
- Weinbaum, C.M., Williams, I.A., & Mast, E.E. (2005) Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *CDC Morbidity and Mortality Weekly Report* 7(8),1-20.
- Williams, R. (2006). Global challenges in liver disease. *Hepatology*, 44 (3), 521–526.
- Wiseman, E., Fraser, M. A., Holden, S. (2009). "Perinatal transmission of hepatitis B virus: an Australian experience." *Medical Journal of Australia*, 190(9), 489–492
- Wolfram, H., & Gerlich, J.** (2013). Medical Virology of Hepatitis B: how it began and where we *are now*. *Virology Journal*, 10, 239-241
- Wong, D.K., Yuen, M.F., Ngai, V.W., Fung, J.A., Lai, C.L. (2006). One-year entecavir or lamivudine therapy results in reduction of hepatitis B virus intrahepatic covalently closed circular DNA levels. *Antiviral Therapy* 11,909–916
- World Health Organization. (2004). Hepatitis B vaccines. *Weekly Epidemiological Record*. 79,255-263.
- Wright, G., & Morar, M. (2010). The genomic enzymology of antibiotic resistance. *Molecular Microbiology* 11,17-23
- Wynne, S. A., Crowther, R. A., Leslie, A. G.(1999). *The crystal structure of the human hepatitis B virus capsid*. *Molecular Cell*. 3,771–780.
- Xiong, W.(2010). "[Clinical efficacy of treating infant cytomegalovirus hepatitis with ganciclovir and impact on cytokines]". *Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi* (in Chinese) 26 (11): 1130–1132.
- Xu, D.Z., Yan, P.U., Choi, B.U. (2002). "Risk factors and mechanism of transplacental transmission of hepatitis B virus: a case-control study," *Journal of Medical Virology*, vol. 67, 1, 20–26
- Yang, H., Lu, S., Liav, Y., You, S., Sun, C., Wang, L., Hsiao, C., Chen, P., Chen, C.(2002) HBeAg and the risk of hepatocellular Carcinoma. *New England Journal of Medicine* , 347,168-74

- Yang, J.D., & Roberts, L.R. (2010). "Hepatocellular carcinoma: A global view". *Nature Reviews Gastroenterology and Hepatology*, 7(8), 448-458.
- Yim, H.J., & Lok, A.S. (2006) "Natural history of chronic hepatitis B virus infection: What we knew in 1981 and what we know in 2005". *Hepatology*, 43 (2), 173-181.
- Yu, M.W., Chang, H.C., & Liaw, Y.F. (2000). Familial risk of hepatocellular carcinoma among chronic hepatitis B carriers and their relatives. *Journal of National Cancer Institute*, 92(14),1159–1164.
- Zerbini, A., Pilli, M., Boni, C., Fiscaro, P., Penna, A., Di Vincenzo, P.,...Missale, G. (2008). "The characteristics of the cell-mediated immune response to identify different profiles of occult Hepatitis B Virus Infection", *Gastroenterology*, 134 (5), 1470-1481.
- Zhou, P., Gross, S., Liu, J., Yu, B., Feng, L., Nolte, J.,...Flavokawain, B.(2010) .The hepatotoxic constituent from kava root, induces GSH-sensitive oxidative stress through modulation of IKK/NF- κ B and MAPK signaling pathways. *Federation of American Societies for Experimental Biology Journal*, 24(12), 4722-4732.
- Zlotnick, A., Cheng, N., Conway, J., Booy, F., Steven, A., Stahl, S., Wingfield, P. *Dimorphism of hepatitis B virus capsids is strongly influenced by the C-terminus of the capsid protein. B Proceedings of the National Academy of Science USA* 35, 7412–7421
- Zoulim, F.(2006). New nucleic acid diagnostic tests in viral hepatitis. *Seminar Liver Diseases*. 26 (4), 309–317

IJSER

IJSER