AFRICAN JOURNAL OF MEDICINE and medical sciences

VOLUME 36 NUMBER 2 JUNE 2007

ISSN 1116—4077

Afr. J. Med. Med. Sci. (2007) 36, 115-118

Viral hepatitis in the aetiogenesis of jaundice in pregnancy at the University College Hospital, Ibadan

A Oladokun[1], JA Otegbayo[2], and AA. Adeniyi[1]
Departments of Obstetrics and Gynaecology[1], and Medicine[2], University College Hospital/University of Ibadan, Ibadan, Nigeria.

Summary
Viral hepatitis is common in Nigeria and may present with jaundice in pregnancy. The objective of this study was to determine the contribution of viral hepatitis among other aetiological factors, to the development of jaundice during pregnancy. Data on viral hepatitis among gravidae with jaundice in pregnancy over a 10-year period from 1st January 1992 through 31st December 2001 were retrieved and analyzed. Fifty-two cases of jaundice in pregnancy were seen among 16,566 pregnancies registered in the hospital over the 10-year period. Of the 52 cases of jaundice in pregnancy, only 48 case records were retrievable, on which this analysis is based. Viral hepatitis (VH) occurred in 1 in 591.6 pregnancies and was diagnosed in 28 (58.3%) cases of jaundice in pregnancy. Other causes of jaundice were malaria 8(16.7%), sickle-cell anaemia in pregnancy 6(12.5%) and sepsis 2(4.2%). Of the 28 patients with viral hepatitis, 8 (28.5%) were positive for HBsAg. The liver function tests (LFTs) were done in 26 of the 28 patients and it showed hyperbilirubinaemia in 24, 11 had serum albumin >3.5g/dl. All had spontaneous vaginal delivery with no maternal death. Complications associated with viral hepatitis were, anaemia 14 (50%), intrauterine growth retardation (14.3 %), intrauterine foetal death 2 (7.1 %), congestive cardiac failure 1 (3.57 %) early neonatal death 1(3.57 %) and 2 (7.1 %) cases of systemic hypertension. Viral hepatitis contributes significantly to jaundice in pregnancy and there is associated fetal and maternal morbidity.

Keywords: *Jaundice, viral hepatitis, pre-term labour, HELLP syndrome, hepatitis B immunization.*

Résumé
L'hépatite virale est commun au Nigeria et peut apparaître avec la jaunisse en grossesse. L'objectif de cette étude était de déterminer la contribution de l'hépatite virale parmi d autres facteurs étiologiques au développement de la jaunisse en grossesse. Les données de l'hépatite virale des femmes enceintes ayant la jaunisse durant une période de 10 ans de janvier 1992 au 31 Décembre 2001 étaient collectés et examinés. Cinquante-deux cas de jaunisse en grossesse étaient vu parmi 16.566 grossesses enregistrées pendant cette période. Sur les 52 cas de jaunisse en grossesse, seulement 48 cas étaient analysés. L'hépatite viral parut sur 1 des 591 grossesse et était diagnostiqué chez 28 (58.3%) des cas de jaunisse e grossesse. Autres causes de jaunisse étaient le paludisme 8(16.7%), l'anémie aux drépanocytaires en grossesse 6(12.5%) et la septicémie 2(4.2%). Sur les 28 patients ayant l'hépatite virale, 8(28.5%) étaient positif au HBsAg. Les tests de fonction hépatiques étaient faite sur 26 patients et démontrait l'hyperbilirubinemie chez 24 et 11 avaient le sérum albumine > 3.5g/dl. Tous avaient un écoulement vaginal spontané sans aucune mortalité maternelle. Les complications associées à l'hépatite virale étaient l'anémie (50%), retard de develepement intra-utérin (14.3%), mort du fétus intra-utérin (7.1%) congestion cardiaque 1(3.75%), mort néonatal precosel (3.57%) et 2 cas d'hypertension systémique. L'hépatite virale contribue significativement a la jaunisse en grossesse et est associée à la souffrance fetale et maternelle.

Introduction

Liver diseases complicate about 1 in 1000 pregnancy with maternal and fetal consequences [1]. Some liver diseases such as obstetric cholestasis, acute fatty liver of pregnancy and the syndrome of haemolysis, elevated liver enzymes, low platelets (HELLP) are well known to be specific to pregnancy states, others such as autoimmune and viral hepatitis are known to be coincidental.

Moreover, interpretation of liver function tests during pregnancy requires some degree of carefulness because of the physiological changes, which alter the usual parameters of liver functions. Alkaline phosphatase is usually increased while serum albumin is lowered and transaminases are either unchanged or lower due to physiological haemodilution [2].

Viral hepatitis is a common disorder in Nigeria and pregnant women are not spared. The

Correspondence: Dr. A. Oladokun, Department of Obstetrics and Gynaecology, University College Hospital, Ibadan, Nigeria. E-mail: oladokun@comui.edu.ng, sinaoladokun@yahoo.com

disease is known not to affect the course of pregnancy except for hepatitis E virus and herpes simplex virus, causing disseminated intravascular coagulopathy, intrauterine death, premature labour and neonatal death [3]. When hepatitis A and B are clinically severe, they could also lead to preterm labour.

Viral hepatitis, especially caused by hepatitis B virus (HBV) is known to be the commonest cause of jaundice from previous studies [4,5]. However, because of the transmissibility of some of the causative agents, especially HBV, to the fetus and the newborn via blood contact and breastfeeding [6], leading to chronic infection and chronic liver disease including hepatic cirrhosis and hepatocellular carcinoma [7,8], it is auspicious to study the contribution of viral hepatitis to jaundice in pregnancy in this environment.

The objective of this study therefore is to determine the contribution of viral hepatitis among other aetiological factors, to the development of jaundice during pregnancy, and to pregnancy outcome.

Materials and methods

The study was a retrospective analysis of viral hepatitis in pregnancy at the University College Hospital, Ibadan, Nigeria. All the records of pregnancies seen at Obstetrics and Gynaecology Department over a 10-year period, from 1st January 1992 through 31st December 2001 were searched for cases diagnosed as viral hepatitis. Their case notes were subsequently retrieved from the Departmental records office of the hospital. Data concerning cases of viral hepatitis, complications of the index pregnancy, foetal and maternal outcomes were obtained and analyzed. Diagnosis of viral hepatitis was based on clinical and laboratory findings. Clinical diagnosis of viral hepatitis was made based on presence of jaundice and other clinical findings such as history of fever, anorexia, vomiting, right upper quadrant abdominal pains, dark urine and tender hepatomegaly. The clinical diagnosis was supported by laboratory tests of liver function and hepatitis B surface antigen.

Results

During the ten-year study period, there were 16,566 pregnancies registered in the hospital, and 52 cases of jaundice in pregnancy were seen. Only 48 case records of jaundice in pregnancy were retrievable. Subsequent analysis in this report is based on the 48 retrieved case records. Viral hepatitis was diagnosed in 28 (58.3%) of cases of jaundice in pregnancy. Other causes of jaundice were malaria 8(16.7%) sickle-cell anaemia in pregnancy 6(12.5%) and sepsis 2(4.2%).

Among the 28 cases of viral hepatitis, 4 (14.3) had previous jaundice, of which 3 were due to viral hepatitis, and 1 had no documented cause. Of the 28 patients with viral hepatitis, 8 (28.5%) were positive for HBsAg. The liver function tests (LFTs) were done in 26 of the 28 patients and it showed hyperbilirubinaemia in 24, with 2 having normal serum bilirubin levels, 11 had serum albumin >3.5g/dl. International normalised ratio (INR) was done in only 6 of the patients. Other parameters of LFTs are as shown in Table 1.

Table 1: Liver function tests among patients with viral hepatitis

Parameter	Range	Mean
Bilirubin (Total)	0.8-26.7	7.24
Bilirubin (Conjugated)	0.1-21.3	4.99
Bilirubin (Unconjugated)	0.3- 9.3	2.67
ALT	7-1875	283.1
AST	23-2418	334.53
Alkaline Phosphatase	118-1228	404.34
Protein (Total)	5.6-8.7	6.88
Albumin	2.3-4.4	3.32
Globulin	2.4-5.4	3.53
INR	0.8-1.14	1.00

All had spontaneous vaginal delivery (SVD). No maternal death was recorded. Documented complications associated with cases of viral hepatitis in pregnancy were, anaemia 14 (50%), intrauterine growth retardation (IUGR) 4 (14.3 %), intrauterine fetal death 2 (7.1 %), congestive cardiac failure 1 (3.57 %), early neonatal death 1(3.57 %), small for gestational age (SGA) 1(3.57 %) and 2 (7.1 %) cases of systemic hypertension. There was no record of hepatitis B immunization in mothers or their newborns.

Discussion

There were 28 cases of viral hepatitis in pregnancy out of the 16,566 registered pregnant women during the study period. This translates to 1 in 592 or 0.17% of pregnancies in the studied population. This however has to be interpreted with a lot of caution

since screening for HBV infection was not done for most of the patients except for those with jaundice in pregnancy. It is also possible that some of those without clinical symptoms or jaundice might be asymptomatic carriers and therefore, HBV infection may occur in a substantial proportion of asymptomatic pregnant women. The study however showed that viral hepatitis is the commonest cause of jaundice in pregnancy as previously documented [4,5], accounting for about two-thirds of the cases of jaundice in pregnancy in this study. This figure is however higher than the finding of Ogunbode in 1978 who did a study at this same hospital and found the prevalence to be about one-third of cases of jaundice in pregnancy [5] but similar to that of Megafu in Eastern Nigeria in 1981 [4]. This might suggest an increasing prevalence of viral hepatitis at our centre and a call to stem the tide.

The history of previous viral hepatitis in 3 of the 28 cases diagnosed as viral hepatitis in the index pregnancy suggest that they actually have chronic form of viral hepatitis, a chronic liver disease that is now known to be ameliorated by immunomodulators and antiviral chemotherapy such as interferon and the nucleoside analogue, lamivudine. Chronic liver disease is known to contribute to adverse fetal and maternal outcome in pregnancy as well as reduced fertility.

Hepatitis B virus infection is endemic in Nigeria with a prevalence approaching twenty percent in some selected normal populations [9] and has been known to be a major cause of both acute [10] as well as chronic viral hepatitis [11,12]. HBV infection, has serious implications in view of the fact that maternofoetal transmission occurs in intrauterine life, peripartum and postpartum. Five percent of fetuses have been reported to be infected in-utero as a result of transplacental haemorrhage [13,14]. It is also well known that infection acquired during the neonatal stage leads to chronicity of infection in 90% of cases [6] with high risk of chronic liver disease later in life. The knowledge of the prevalence of HBV infection should mandate antenatal screening of all gravidae, as has been suggested in developed countries [15]. Furthermore apart from pre-natal screening for HBV infection, it has also been made mandatory for vaccination of negative pregnant women and passive and active immunisation of neonates of HBsAg positive mothers [16]. Liver function test parameters especially serum albumin are known to be deranged in normal pregnancy due to the physiological haemodilution that occurs especially in the third trimester, giving rise to lower values [2]. This was demonstrated in this study with 15 of the 26 patients that had LFT showing hypoalbuminaemia with serum albumin less than 3.5g/dl. All the patients but one had raised levels of alkaline phosphatase >150 IU/L. This is in keeping with the known fact that placental alkaline phosphatase tends to contribute to the normal serum alkaline phosphatase in pregnancy. The Prothrombin time (INR) that was carried out in only 6 of the patients tend to portray the underestimation of this test which is in fact the best test of liver function due to the fact that many of the clotting factors have short half lives of hours, which makes the test of value in following closely the functional integrity of the liver.

Generally, in developed countries, severity of hepatitis in pregnancy is said to be similar to that in the non-pregnant state. However, in developing countries co-existence of parasitic disorders and malnutrition usually worsen the outcome.

The complications noted to be associated with cases of viral hepatitis in pregnancy in this study, such as anaemia, intrauterine growth retardation (IUGR), intrauterine foetal death, congestive cardiac failure, systemic hypertension, small for gestational age (SGA), and early neonatal death may just have been unrelated to the viral hepatitis. Ogunbode, however documented in his study that hepatitis had a deleterious effect on the outcome of pregnancy with the effect being directly related to the severity of the disease, especially when there was associated pyrexia [5]. These findings call for close maternal and foetal monitoring during pregnancy in those who develop viral hepatitis during pregnancy in developing countries. It is remarkable that there was no record of hepatitis B immunization in mothers and their newborns in this study. This suggests a very low awareness about HBV and its acute and chronic sequelae, which include liver cirrhosis and hepatocellular carcinoma. There is an urgent need to heighten the campaign against the identified risk factors for acquisition of the virus [17] as well as campaign for mass vaccination to prevent the obstetric and other long-term complications known to be associated with HBV infection.

It is concluded that viral hepatitis is the commonest cause of jaundice in pregnancy in the studied group with some associated adverse foetal outcome, but without a remarkable maternal outcome. There is low hepatitis B vaccination status

among pregnant women and their newborns. Hepatitis B immunisation needs to be emphasised in antenatal care.

References

1. Williamson C and Nelson-Piercy C. Liver disease in Pregnancy. Br. J. Hospital Med. 1997; 58:213-216.
2. Girling JC; Dow E and Smith JH. Liver function tests in pre-eclampsia: importance of comparison with a reference range derived for normal pregnancy. Br. J. Obstet Gynaecol. 1997; 104:246-250.
3. Borhanmanesh F; Haghighi P; Hekmat K *et al.* Viral hepatitis during pregnancy: Severity and effect on gestation. Gastroenterology. 1973; 64: 304-312
4. Megafu U. Jaundice in pregnancy aetiology, management and mortality at Enugu, Nigeria. East Afr Med J. 1981; 58:501-509.
5. Ogunbode O. Jaundice during pregnancy in Ibadan, Nigeria. Int J Gynaecol Obstet. 1978: 16:289-292.
6. Pastorek JG. Hepatitis B. Obstet. Gynae Clin North Am. 1989;16:645-647.
7. Chen DS and Sung JL. Hepatitis B virus infection and chronic liver disease in Taiwan. Acta Hepatogastroenterologica. 1978; 25:423-430.
8. Popper H; Gerber MA and Thung SN. The relation of hepatocellular carcinoma to infection with hepatitis B and related viruses in man and animals. Hepatology. 1982; 111s-119s.
9. Nasidi A, Harry TO, Vyazov SO, *et al.* Prevalence of hepatitis B infection markers in representative areas of Nigeria. Int J Epidemiol. 1986;15:274-276.
10. Ola SO, Otegbayo JA, Odaibo GN, *et al.* Serum hepatitis C virus and hepatitis B surface antigenaemia in Nigerian patients with acute icteric hepatitis. West Afr J Med. 2002; 21:215-217.
11. Ojo OS, Akonai AK, Thursz M, *et al.* Hepatitis D virus antigen in HBsAg positive chronic liver disease in Nigeria. East Afr Med J. 1998;75:329-331.
12. Malecki JM; Guarin O; Hulbert A; *et al.* Prevalence of hepatitis B surface antigen among women receiving prenatal care at Palm Beach County Health Department. Am. J. Obstet. Gynae. 1986; 154: 625-626.
13. Baddour LM; Bucack VA; Somes G; *et al.* Risk factors for Hepatitis B virus infection in black female attendees of a sexually transmitted disease clinic. Sexually Transmitted Diseases. 1988; 15:174-176.
14. Ohto H; Lin H-H; Kawana T; *et al.* Intrauterine transmission of hepatitis B virus is closely related to placental leakage. J. Med. Virol. 1987; 21: 1-6.
15. Immunisation Practices Advisory Committee. Prevention of perinatal transmission of hepatitis B virus: pre-natal screening of all pregnant women for hepatitis B surface antigen. Mortality and Morbidity Weekly Report. 1988; 37: 341-353.
16. American College of Obstetrics and Gynaecology. Guidelines for hepatitis B virus screening and vaccination during pregnancy. ACOG Committee Opinion Number 111. Washington, DC: ACOG 1992.
17. Otegbayo JA, Fasola FA and Abja A. Prevalence of hepatitis B surface and e antigens, risk factors for viral acquisition and serum transaminase among blood donors in Ibadan, Nigeria. Trop Gastroenterol. 2003;24:196-197.

Received: 28/12/04
Accepted: 02/05/07