Hepatitis C Virus Infection in Nigerians

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SUMMARY

Background: Hepatitis C virus is a chronic life long infection in the majority of patients who are infected with the virus. Not much is known and written/published about this virus in Nigeria.

Objective: To asses the status of hepatitis C virus infection in Nigeria.

Materials and method: Sources of information were mainly from published works in and outside Nigeria. The information was extracted over a period of 12 months from January to December 2009.

Results: So far the prevalence of hepatitis C. virus infection is increasing in Nigeria, ranging from 4.7-5% in Ilorin, to 5.3-6.6% in Enugu, to 11% in Ibadan and 20% in Benin. Children and adults are all at risk of being infected especially sickle cell disease patients. Others include those who are exposed to the common risk factors like Blood transfusion, haemodialyisis, recycling of syringes and needles, sexual promiscuity.

Conclusion: Reduction in the Hepatitis C virus infection could be achieved by Health education campaign of the general public and by support from government and non-governmental organizations for the to provision of antiviral and immunostimulatory drugs free of charge for those already infected.

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INTRODUCTION

Historically, patients with hepatitis, without serological evidence of hepatitis A or B infection, initially described in recipient of blood or blood products were classified as non-A, non-B hepatitis. This was only possible following the development of diagnostic serological tests for hepatitis A and B in 1965 and 1973 respectively.[1] In 1989, an agent of the non-A, non B viral hepatitis was identified as RNA virus with immunological specificity for transfusion associated non- A, non – B hepatitis. Among complementary DNA fragments (CDNA) cloned in *Escherichia coli* from the pellets of chimpanzee plasma with unusually high infectivity, one clone expressed protein that reacted with antibody in convalescent serum, but not pre-illness serum from chimpanzees with experimentally induced non-A, non-B hepatitis. The virus seemed to be a single stranded RNA virus with a genome of appromateely10,000 nucleotides. It had no homology with HBV, retroviruses or other hepatitis viruses. The agent was named hepatitis C virus (HCV) by Choo and his co-workers in 1989.[2] The clinical importance of HCV infection is due to viral persistence in approximately 85% of those infected and the significant risk of subsequent development of chronic irreversible liver damage.[3]

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STRUCTURE OF HCV

HCV is an RNA virus that belongs to the family of flaviviruses. The natural target of HCV are hepatocyts and possibly B-lymphocytes. The virus genome is a single strand of positive sense RNA encoding three structural and seven non structural proteins.[3] The genome is enclosed in a protein coat, which is wrapped in a lipid envelope derived from host cell. The viral particle consists of an envelope derived from host membranes, into which are inserted the virally encoded glycoproteins (E1 and E2) surrounding a nucleocapsid. Sequence variation of the genome occurs mainly in the NS2, E1 regions whereas a high degree of conservation is observed in the non-coding C, NS3, NS4 and NS5 regions. It also contains regions from which peptides have been produced for assays. The structure is shown in fig 1[4] below.

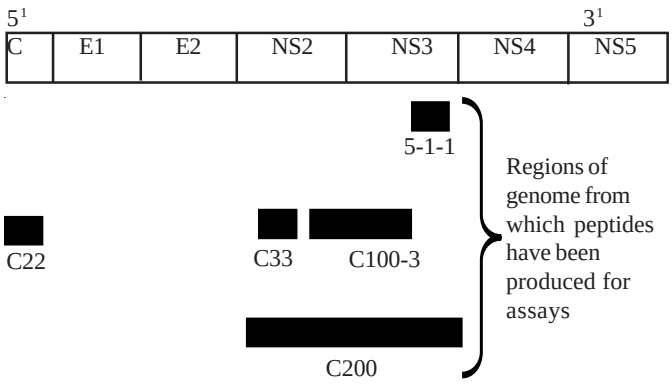

Fig 1: Schematic diagram of hepatitis C virus. RNA coding regions [4] (C = core proteins; E = Envelope; NS = Non – Structural proteins)

EPIDEMIOLOGY

Information on the epidemiology of this virus in Nigeria is limited. Nevertheless it has long been suspected that it may be endemic. A pilot study done in Nigerian adults and children using second generation of enzyme immunosorbent assays (EIAs) kit gave an average sero- prevalence of 8%[5], while another study on adult blood donors in Nigeria using EIAs kit of an unspecified generation reported a prevalence rate 12.3%[6]. However, a study of adolescent and adult patients with sickle cell Anaemia (SCA) in Benin by Mutimer *et al* using second generation EIAs kit showed 20% prevalence rate.[7] This relatively high prevalence was attributed to cross-reactivity with *Escherichia coli*.[7] Another study in Lagos by Lesi and Kehinde[8] conducted among children and adults with SCA using third generation EIAs kit showed 5% prevalence. Adewuyi[9] in Ilorin using EIAs kit of an unspecified generation documented 5% prevalence among 60 multi- transfused SCA patient and 4.7% prevalence among 64 non transfused SCA patients. Ejiofor *et al* [10] in Enugu using second generation EIAs kit reported 6.6% and 5.3% prevalence rates respectively among transfused and non-transfused children with SCA. Also another study in Ibadan ,[11] conducted among doctors and dentists using EIAs kit of an unspecified generation recorded a sero- prevalence of 11%. Ejiofor et al [12] in socio demographic differences in the distribution of HCV antibodies among children with SCA in Enugu documented that HCV infections occur more in 1-6 years and 13-18 years age groups which was equally reported by Lesi and Kehinde in lagos. Ejiofor *et al* [12] also noted that more males than females were infected though their difference was not statistically significant. They also noted that HCV infections were found more in lower socio-economic class than other social classes. None of the other reviewed studies[7, 8,9] mentioned any gender or social class difference in the prevalence of HCV infection. This may suggest a chance finding and larger studies may be required to further throw light on this observation.

TRANSMISSION OF HCV

HCV is transmitted parenterally. The most common risk factor for HCV infection in developing countries like Nigeria is transfusion of unscreened blood or plasma derived products. [13] Other potential risk factors include re-usage of syringes and needles, intranasal cocaine use, tattooing, body piercing, accidental needle-stick injury[14,15] and sharing of household items such as nail clippers, razor blades and tooth brushes.

Needle-stick injury: Accidental needle stick injury in healthcare workers may lead to transmission of the virus. The estimated risk of transmission of HCV as a result of needle stick injury is 1.8%[16].

Perinatal transmission: Perinatal transmission of HCV infection occurs in approximately 3-5% of infants born to women infected with HCV.[17] The risk of transmission is increased when the mother is HIV positive or when there is a high HCV viral load.

Sexual transmission: sexual transmission of HCV infection remains unresolved and probably accounts for less than 5% of cases[15]. Risk factors for sexual transmission include multiple sex partners, prostitution and rectal intercourse.

Other factors: Other groups at risk include sickle all anemia (SCA) patients, those on haemodialysis or who receive blood clotting factor concentrates as in hemophiliacs, those who receive transplants or exposed to unsafe medical practices like re-usage of syringes and unsterile surgical procedures as can be found in alternative medical practices.[18] See table below

Table I: Potential risk factors for HCV infection[15]

Common	Uncommon
- Blood transfusion	- Intranasal cocaine
- Haemodialysis/Intravenous drug use	- Body piercing
- Recycling of syringes and needles	- Tattoos
- Sexual transmission	- Sharing of household items
- Perinatal transmission	- Accidental needle injury
- Haemophilia	
- Organ/Tissue transplant	

DIAGNOSTIC INVESTIGATIONS IN HCV INFECTION

Various tests are available for the diagnosis and monitoring of HCV infection. Tests that detect antibody against the virus include the enzyme immunosorbent assays (EIAs), which contain HCV antigens from the core and nonstructural genes, and the recombinant immunoblot assays (RIBAs) [19,20] . The same HCV antigens are used in both EIAs and the RIBAs. Target amplification techniques using either polymerase chain reaction (PCR) or transcription-mediated amplification (TMA) have been developed to detect HCV RNA. Liver biopsy can provide direct histologic assessment of liver injury due to HCV but cannot be used to diagnose HCV infection. After initial exposure, HCV RNA can be detected in blood in 1 to 3 weeks and is present at the onset of symptoms. [21] Antibodies to HCV are detected by enzyme immunoassay (EIA) in only 50 to 70% of patients at the onset of symptoms, increasing to approximately 90% of these after 3 months. Within an average of 2 to 8 weeks, liver cell injury is manifested by elevation of serum alanine aminotransferase (ALT).

COMPLICATIONS OF HCV INFECTION

HCV is hepatotropic and has profound effect on the liver. Acute HCV is symptomatic in a minority of cases and usually runs a mild clinical course, with only one third or fewer patients being jaundiced and many are completely asymptomatic. The disease is rarely fulminant but this has been reported to occur[22,23]. Rather, indolence and chronicity are the hallmark of HCV. Approximately 15-30% of patients exposed to HCV recover spontaneously while the remaining 70%-85% develop chronic infection[24]. Most patients with HCV infection appear to have a mild to moderate histologic disease[25-29]. Cirrhosis may develop in as many as 15-30% of infected patients[15]as shown in fig 2. Factors that have been suggested as predictive of complications/ severe or rapidly progressive disease are older age, immuno deficiency concurrent alcohol abuse.[30] Other factors include male sex, co- infection with either hepatitis B or HIV. In some series, certain HCV strains and highly degree of genetic heterogeneity[31] as shown in table II. The extent to which they influence disease complication/progression however is not known for sure.

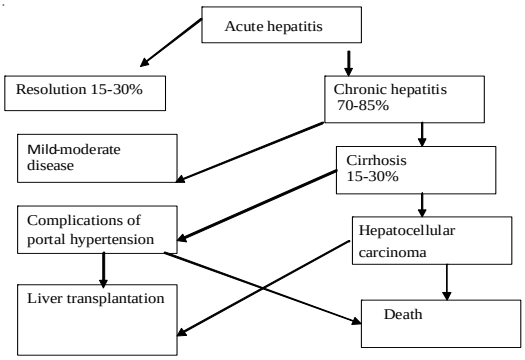

Fig 2: Natural history with complications of the HCV[15]

Table II: Factors Affecting Disease Progression/ Complications[32]

Adverse effect	No effect
- Alcohol use	- Serumaninotransferase level
- Disease acquisition at age greater than 40yrs	- Viral load
- Male sex	- Genotype
- HBV co-infection	- Mode of transmission
- HIV co-infection	

HCV can lead to a broad spectrum of liver disease. Patient may develop mild disease as evidenced by mild inflammation and mild fibrosis. Others may develop increasing amounts of inflammation and or fibrosis which can lead to the development of significant fibrosis or cirrhosis. These in addition to end stage liver disease (ESLD) and Hepatocellualr carcinoma (HCC) are the most important sequale of chronic HCV infection.[15] Other complications of chronic HCV infection include some extra hepatic syndromes considered to be immunologic in origin like rheumatoid symptoms, keratoconjuctivtis, lichen planus and glomerulonephritis.[15]

TREATMENT OF HCV INFECTIONS

Since 15-30% of patient develop cirrhosis over 20 years[33] , it would be useful to only select this group of patients as potential candidates for treatment. Unfortunately it is not possible to accurately predict which subgroup of patients will progress. As guidelines, the United States National Institute of Health (NIH) and Europe Consensus Development Conference[34], suggest that patients with elevated aminotransferase levels, detectable serum HCV-RNA, and chronic inflammation with some degree of fibrosis should be offered therapy[35]. The primary aim of therapy in the patient with HCV is to achieve a sustained virologic response, which is defined as undetectable HCV RNA 6 months after termination of antiviral therapy. Secondary goals of antiviral therapy include improvement in histology and quality of life and the prevention of Hepatocellular carcinoma. [15] Several important therapeutic advances have occurred, particularly with the introduction of pegylated interferon in combination with ribavirin therapy[36]. Combination therapy results in better treatment responses than monotherapy. The highest response rates have been achieved with pegylated- interferon in combination with ribavirin.

CONTROL OF HCV INFECTION

The are four management options for dealing with chronic HCV in developed countries.[3] They include the use of (1) immune response modifiers (i.e interferons) (2) antiviral agents (i.e ribavirin) (3) combination therapy with interferon and ribavirin and (4) liver transplantation, if the above chemotherapy fails But in developing countries like Nigeria where the rate of poverty is high, most patients may not be able to afford the treatment modalities because the drugs are expensive. The most logical thing to do is to prevent contracting the HCV. One of the preventive strategies is the use of vaccine as with HBV infection, but there is no vaccine against HCV [37,38] Research is in progress, but the mutability of HCV genome complicates vaccine development.[37] Immunoglobulin has not proved to be of benefit.[31] Immunoglobulin produced in the United States of America does not contain antibodies to HCV,[38] because blood and plasma donors are screened for antibodies to HCV and excluded from donor pool.

However, because of the problems associated with vaccine development and non-benefit of Immunoglobulin, HCV infection in Nigeria can be prevented or drastically reduced through health education of the people on different routes of transmission of the HCV and other preventive measures. Such measures include careful handling of blood and body fluid since they are potentially infectious. Also communal sharing of blades/sharp instruments used for shaving, barbing, manicure and body piercing/cutting should be discouraged. Individuals infected with HCV should not donate blood, organs, tissues or semen[34]. Safe sexual practices including the use of Latex condoms is strongly encouraged for individual with multiple sexual partners.[34]

Furthermore, adopting the WHO [37] recommendations for the prevention of HCV will also help. These include,

- Screening and testing of blood and organ donors for HCV.
- Virus inactivation of plasma derived products.
- Implementation and maintenance of infection control practices in the health care settings, including appropriate sterilization of medical and dental equipment and safe disposal of sharps.
- Promotion of behaviour change among the general public and health care workers to reduce over use of injections and to use safe injection practices.
- Risk reduction counseling for the persons with high-risk drug and sexual practices.

Moreover, since both HIV and HCV share common risk factors and mode of the transmission, it will be equally important to incorporate information on HCV risk factors into HIV/AIDS intervention strategies in Nigeria as an alternative. On the hand, to drastically reduce the prevalence of this deadly disease in Nigeria, nationwide campaign should be done on national immunization days as is the case with polio immunization to help create awareness of this HCV infection.

Finally as is the case with HIV, drugs for the treatment of HCV infection should be provided free or subsidized by government and non-governmental organizations. These drugs, namely, ribavirin and interferon will reduce replication and viral

load over time thereby reducing the transmission of the virus, hence the morbidity and mortality associated with it.

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