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Genotypic Profile of Hepatitis C Virus (HCV) in Patients Attending the Medical Outpatient Department in Bingham University Teaching Hospital Jos Nigeria for Chronic HCV Infection

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Abstract **INTRODUCTION**: HCV is recognized as the major cause of transfusion associated and sexually transmitted sporadic chronic non-A non-B hepatitis. There is a high degree of genetic variability from HCV genomes isolated from infected patients. Currently, HCV isolates are classified into at least six major genotypes and numerous sub- genotypes. The genetic diversity of HCV and the clinical and virological relevance of HCV genetic classification schemes remain important areas of active research. **OBJECTIVES:** The objective of this study was to determine the genotypic profile of hepatitis C virus (HCV) in patients who are infected with chronic HCV with or without liver cirrhosis and hepatocellular carcinoma, receiving treatment at the medical outpatient department (MOPD) of the Bingham University Teaching Hospital Jos Nigeria with a view to seeing which of these genotypes is more prevalent. **METHODS:** This prospective cohort study enrolled patients who were clinically diagnosed to have chronic HCV infection and subsequently confirmed by polymerase chain reaction (PCR) using the light cycler. Patients attending the clinic from December 2012 to December 2014 who had all the relevant investigations done were enrolled in the study. This was regardless of whether they were profiled for commencement of treatment or not due to disease stage. **RESULTS:** A total of 48 patients were enrolled for the study during the period. Out of this figure, genotype 1 patients accounted for 34 (70.8 %) to emerge the leading genotype in the centre. This was followed by genotype 4 with a very low value of 7(14.6 %) as the second while genotype 2 had 6 (12.5 %) and genotype 3 had only 1 (2.1 %) patient. **CONCLUSION:** The study has revealed that HCV genotype 1 is the most prevalent among the population studied followed by genotype 4 while other genotypes 2 and 3 were also encountered but with lesser prevalence.

Keywords: *viral hepatitis C, chronic infection, genotypes*

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1. Introduction/Review of Literature

Chronic viral hepatitis is a leading cause of morbidity and mortality in sub-Saharan Africa and in Nigeria in particular. The commonest cause of this inferno is hepatitis B virus (HBV) infection followed by HCV. The prevalence of HCV is 2-4% in Nigeria compared to that of HBV which averages 19% [1].

Hepatitis C virus infection is increasingly becoming very important either as a mono-infection or co-infection with HIV or HBV with faster rate of disease progression. Globally it is estimated that more than one million new cases of infection may probably occur every year and current postulate suggests that HCV may be more prevalent than HBV in some parts of the world probably due to under-diagnosis as a vast majority of the infected people are in the rural areas where needed medical facilities do not exist or are simply not affordable [2].

In the United States alone, nearly four million persons are infected while in Nigeria this figure may be as high as 6.8 million. Acute new HCV infection seems difficult to be documented because they are rare and also due to low index of suspicion among the clinicians [3]. Currently, HCV is a leading cause of morbidity and mortality and is also the leading reason for liver transplantation in the United States [3].

The economic burden of HCV/HBV infection is enormous, putting a lot of stress on the society to the

extent that only the very financially buoyant individuals may be able to afford the treatment of HCV infection full term. Even now, the treatment of HCV infection is rapidly changing such that an uninformed clinician may lose track of current trend of management [4]. The current trend has moved from the initial standard of care using pegylated interferon and weight-based ribavirin to an interferon free regime using the direct acting antivirals alone or in combination with a shorter duration of treatment. The nucleus of these rapid changes revolves around the genotypic profile and molecular characteristics of this virus. There is therefore a need to profile every infected patient genotypically before commencement of any treatment option.

At present, 11 different HCV genotypes have been reported from various parts the world, with genotype 1 through 6 been the most frequently encountered and discussed. Genotype 1 infections are considered among the most difficult to treat, due to longer treatment duration and higher rate of non- response or relapse and has been said to be rare in Africa. Genotype 2 is the second most common HCV genotype in the U.S, genotype 3 is endemic to Southeast Asia and unevenly distributed throughout Australia, India and other parts of the Far East. Genotype 4 is most common in Africa due to the high prevalence reported in Egypt; it is also common in the Middle East and several eastern European countries [5]. Genotype 5 is most commonly seen in southern Africa, genotype 6 is common in southern China, Hong Kong and other Southeast Asian countries while genotype 7 was reported in 2014 from Thailand and the Democratic Republic of Congo. Also, genotypes 9, 10 and 11 have been identified, although infections have been relatively isolated within Vietnam and parts of Indonesia.

From the above, it can be seen that various HCV genotypes have been reported in different parts of the world. In Nigeria, genotypes 1,2,3 and 4 has been reported from various laboratories. There is likely a regional variation in the prevalence of a particular genotype similar to the same variation that affects the distribution of viral hepatitis in the country with increasing prevalence as you move from the southern to the northern part of the country. This is still to be determined as well as the likely effect this finding will have on the existing treatment protocols. Mixed genotypic appearance has been noted as well among the HCV reports. How this too will affect treatment outcome is also still to be determined.

2. Method

This study was a prospective study which started from December 2012 to December 2014 when proper documentation of the cases began. Patients who tested positive to HCV antibody and were attending the Medical Outpatient Department of the Bingham University Teaching Hospital Jos, Plateau state Nigeria, were enrolled and profiled for the possibility of treatment. After detailed clinical evaluation which included clinical history and physical examination, the patients who initially tested positive to HCV antibody were given a consent and filled laboratory forms requesting for HCV RNA viral load and HCV genotype testing in the referred lab. They were then given a three week appointment when their results would be made available by the lab.

Inclusion in the study required having both HCV RNA viral load and HCV genotypes. Some patients who initially were positive for HCV antibody but had a negative HCV RNA were dropped from the study as there was no evidence of viral particles. All other relevant investigations were done including the liver function tests, thyroid function tests, complete blood counts, clotting profile and abdominal ultrasound scan.

The HCV RNA viral load and HCV genotypes were done in DNA laboratory using the ABI 7900 and Beckman Coulter respectively. The relevant data that were extricated for the purpose of this paper included the age, sex, viral load and viral genotype. The data obtained was entered into the system and analysed using the IBM SPSS 20. A value of $p < 0.05$ was considered significant.

3. Results

A total of 48 patients were enrolled during the period of study out of the 62 patients that were initially sent for HCV RNA viral load and genotype. Of this figure, 28 (58.3 %) were males while 20(41.7 %) were females as shown in Figure 1 below. (Figure 1)

The age range is from 16 years to 70 years with a mean of 50.54 years. The genotype I patients had a mean age of 51.79 years as compared to the genotype 4 group with a mean age group of 53.14 years as shown in Table 1 below. (Table 1)

From the study, 34 (70.8%) out of the 48 patients were genotype I followed by genotype 4 with a total of 7 (14.6 %), genotype 2 with a total of 6 (12.5 %) and genotype3 with a total of 1(2.1 %) as shown in Figure 2. (Figure 2)

The mean HCV RNA viral load for genotype 1 patients was 1,460,753.56 IU/ML, genotype 2 patients had 608,753.83 IU/ML, genotype 3 had 1, 042,280.00 IU/ML and for genotype 4 it was 19,315,260.57 IU/ML respectively also as shown in Table 2. (Table 2)

Table 1. Showing frequency distribution of the ages

HCV GENOTYPE	N	Mean	Std. Deviation	Std. Error
1	34	51.79	11.888	2.039
2	6	40.50	15.859	6.474
3	1	50.00	.	.
4	7	53.14	17.034	6.438
Total	48	50.54	13.343	1.926

Table 2. Showing frequency distribution of HCV genotypes and mean HCV RNA viral load

HCV GENOTYPES		Frequency	%	MEAN VIRAL LOAD
	1	34	70.8	1460753.56
	2	6	12.5	608735.83
	3	1	2.1	1042280.00
	4	7	14.6	19315260.57
	Total	48	100.0	3949315.42

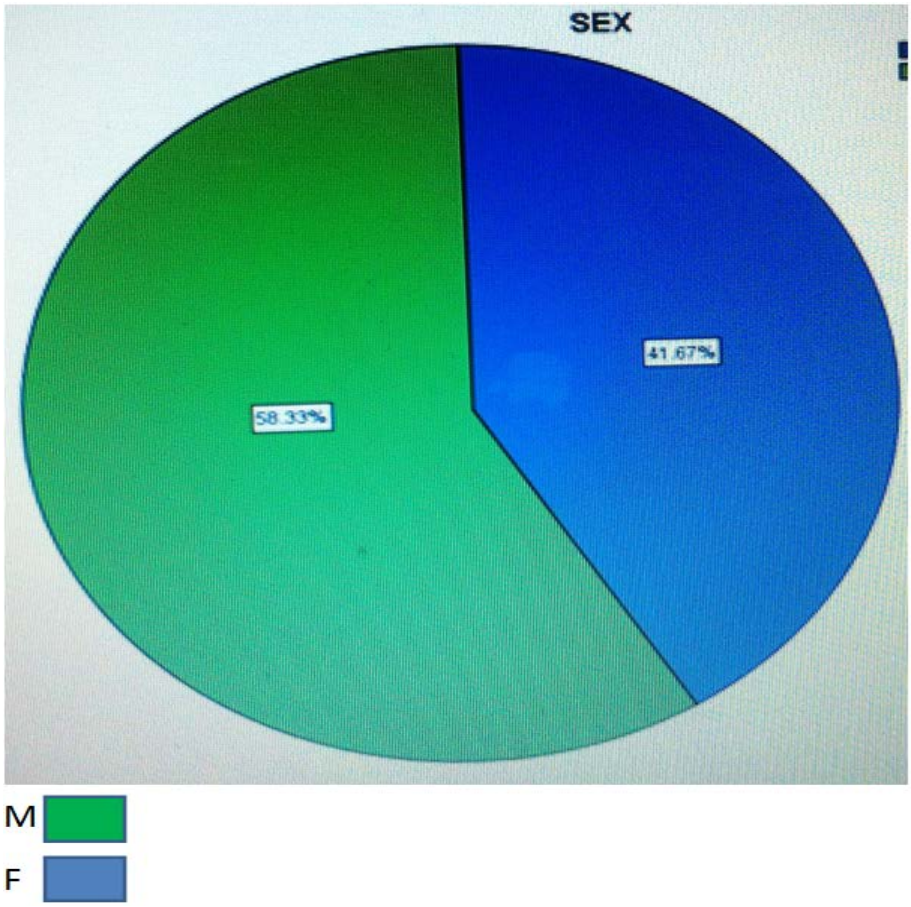

Figure 1.

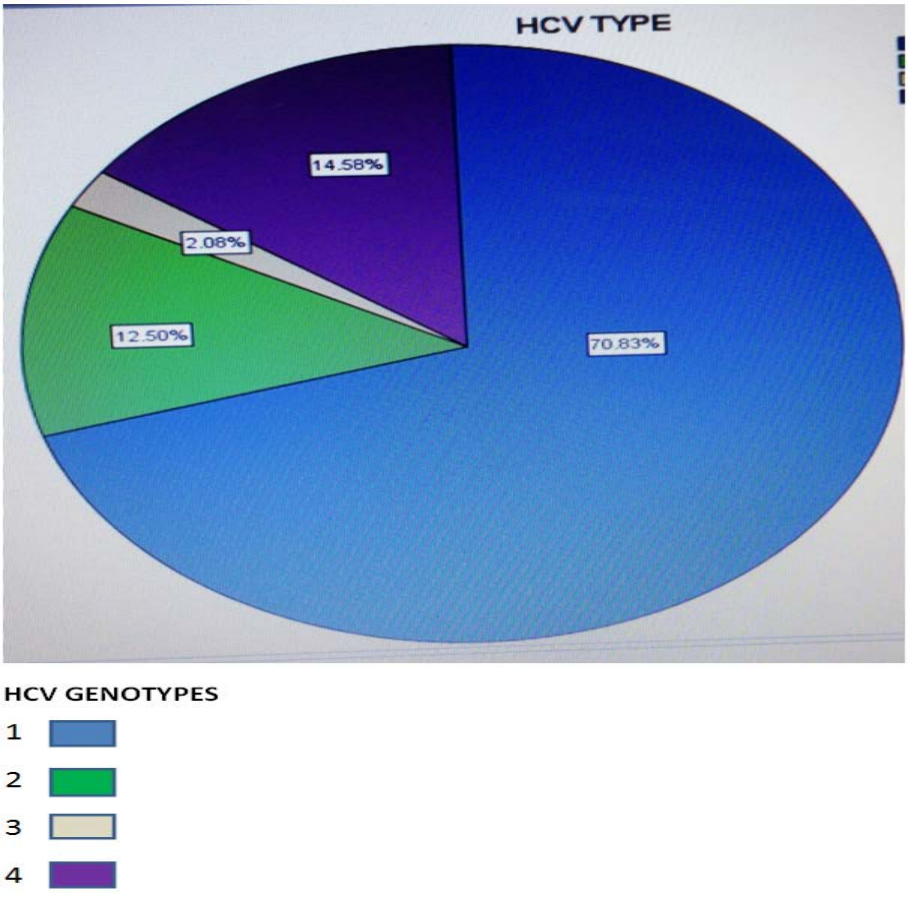

Figure 2.

4. Discussion

From the study, HCV1 is the most prevalent genotype in the population studied. This is contrary to the initial reports citing HCV4 as the most prevalent [6]. The prevalence of HCV4 may actually be limited to North Africa and in particular Egypt from where such reports initially emanated [6]. The previous survey conducted in the country did not report the genotypes of HCV so whether this is a true reflection of a National finding is still to be determined. This is more likely though due to the fact that the reported prevalence of HCV is also different from one region to the other in keeping with the previous reports that geographical variations may exist in the distribution of HCV genotypes [7].

The small population studied is due to the fact that the prevalence of HCV is very low in this part of the country [8]. Also the cost of HCV RNA viral load and HCV genotype is enormous and still beyond the reach of most people affected by the disease. There is also no governmental support for the evaluation of HCV RNA and genotyping as it is not covered by the National Health Insurance Scheme.

The result also showed that HCV1 infection is commoner in males compared to females. This finding is similar to previous surveys reported in the literature [9]. This may be because more males visit the hospital compared to females and that the females may not be able to visit the hospital without the approval of their husbands. The impact of the economic burden on the family may also be a factor as it may be more desirable to keep the head of the household healthy or alive if he is the sole provider for the family as it is in every traditional African setting.

The HCV1 and HCV4 patients appear to be older compared to the other genotypes suggesting the chronicity of the infection and also that the virus might have been around a long time without discovery due to paucity of facility.

Identification of HCV genotype is thus very important in several ways. It has been shown in the literature that HCV induced disease progression may be affected by the genotype as well as the treatment duration, non-response, relapse, course of cirrhosis and risk of hepatocellular carcinoma. Also knowing the genotype of the virus can assist in tracking the specific viral type in the event of an outbreak thereby making for a rapid diagnosis and prompt planning of management strategies and allocation of resources. This will prevent the unnecessary exposure of patients to medications not needed and may also prevent undue side effects and strain on the too little resources made available in our setting.

In a study by Amoroso et al [10], it was shown that the rate of evolution to chronicity after acute exposure to HCV was 92% in patients exposed to HCV genotype 1b infection, compared with 33% to 50% in patients exposed to other genotypes. These data provided evidence that viral factors, including the HCV genotype, may potentially play an important role in the development of chronic infection following acute exposure to HCV.

Similarly it has been shown that severe complications such as cirrhosis and hepatocellular carcinoma can occur over a short period in some persons whereas others have no complication despite a much longer period of infection. Therefore, it is likely that viral or host factors, including the infecting HCV genotype, contribute to these variations in the natural history among infected patients. In patients with chronic HCV, infection with genotype 1b is reportedly associated with a more severe liver disease and a more aggressive course than is infection with other HCV genotypes [11,12].

5. Conclusion

It can be concluded from this study that HCV1 is more prevalent in our centre and more work need to be done to see if this is also true for the other five zones in the country. HCV genotype 4 was not as most prevalent as previously reported and this may indicate a limitation of its significantly higher prevalence only to the Northern part of Africa and specifically to Egypt.

Conflict of Interest

The author has declared no conflict of interest, we have not obtained any funding from any company for this work.

What Is Already Known about This Topic

1. CHRONIC VIRAL HEPATITIS IS A GLOBAL PROBLEM
2. HEPATITIS C IS AMONG THE LEADING CAUSES OF LIVER TRANSPLANT
3. TREATMENT OF HEPATITIS C IS VERY DYNAMIC

What This Topic Adds

1. HEPATITIS C MAY NOT BE A SERIOUS PROBLEM IN WEST AFRICA
2. HEPATITIS C GENOTYPE 4 MAY NOT BE VERY COMMON IN NIGERIA
3. DIRECTED TREATMENT MAY BE PROMPT AND COST EFFECTIVE.

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