

FREQUENCY OF HEPATITIS C VIRUS GENOTYPES IN THE NORTH OF PAKISTAN

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ABSTRACT

Background: The prevalence of hepatitis C infection is high in Pakistan. Up till now six genotypes have been identified. Genotype 3 is the most prevalent form in Pakistan. However, studies have shown regional variations in the prevalence of different genotypes. The aim of this study was to find out the prevalence of major genotypes of hepatitis C in the North of Pakistan.

Material & Methods: This descriptive cross-sectional study was conducted from July 2010 to July 2013 at MMT Hospital D. I. Khan and Ibrahim Hospital & Trust Peshawar, Pakistan. Patients blood samples positive for Anti-HCV were then subjected to PCR for HCV RNA. Genotype determination was done using ROTOR Gene TM. Data was recorded in tables and analyzed by using SPSS version 18.

Results: A total of 537 patients meeting the inclusion criteria, aged between 16 to 65 years, were included in this study, out of which 282 (53.1%) and 255 (46.9%) were males and females respectively. Regarding HCV genotyping; 355 (66.11%) were type 3a, 14 (2.61%) 3b, 40 (7.45%) type 2a, 5 (0.93%) types 2b, 1a and 1b each, 9 (1.67%) patients mixed types 2a and 3b, 3 (0.56%) were combined 3a and 3b and 101 (18.81%) were un-type able.

Conclusion: Type 3 is the most prevalent HCV genotype in the North of Pakistan followed by type 2. The type 1 genotype is less prevalent in the North as compared to the rest of Pakistan. Because of the more prevalence of type 3 & 2, we can safely recommend shorter durations of antiviral therapy with better viral clearance rates.

KEY WORDS: Hepatitis C; Genotypes; Hepatitis C virus; Hepatitis.

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INTRODUCTION

Viral hepatitis is an important healthcare concern worldwide. Of the six main viruses causing the acute form of the disease, Hepatitis C virus (HCV) causes a prolonged chronic form of the condition in susceptible patients¹. With 170 million people chronically affected worldwide², the prevalence in Pakistan ranges between 4-7%.³This high rate has resulted in an increased number of patients with previously undetected HCV infection presenting with chronic liver disease and ultimately cirrhosis liver. Additionally, it caused almost 69% of all ICU admissions and deaths in our region.⁴

Hepatitis C virus is being classified into eleven

types of genotypes out of which six different genotypes have been identified as major types of HCV to date.⁵ The significance of knowing the various genotypes of HCV causing infection lies in the duration of treatment required to successfully eradicate the virus. Determination of genotype is strongly recommended prior to treatment initiation so as to better predict the expected virus clearance rates and the empirical duration of treatment. The recommended duration for treatment of genotype 2 and 3 is 24 weeks while it remains 48 weeks for genotype 1 infected patients.⁶⁻⁸

Genotype 3 is considered to be widely prevalent in Pakistan.⁹ A study in Bahawalpur revealed that other genotypes besides genotype 3 may be more prevalent in different regions and villages across the country.¹⁰

We decided to conduct this project because while doing comprehensive review of literature, we concluded that all the available studies were carried out mostly in the South of Pakistan with people having different ethnic backgrounds than those in the North of Pakistan. These differences may result

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in varied possible susceptibilities or resistance patterns to different genotypes in the local population. This belief was further strengthened by the fact that genotype facilities available in this part of Pakistan are very scarce and expensive. Most of the patients for HCV infections are treated without knowing the HCV genotypes involved. Carefully collecting, analyzing and then reporting our local data will help all the treating doctors of the expected HCV genotypes and the treatment outcomes.

The aim of this study was to find out the prevalence of major genotypes of hepatitis C in the North of Pakistan.

MATERIAL AND METHODS

It was a descriptive cross-sectional study carried out over three years between July 2010 to July 2013 at Mufti Mehmood Teaching Hospital D.I.Khan and private consulting clinic in Ibrahimi Hospital and Trust, Dabgari Gardens, Peshawar, Pakistan. Convenience sampling was done. All adult patients of either sex between 16 to 65 years of age suffering from chronic HCV infections were included. Well informed written consent was taken from all the participating individuals. Both treatment naïve as well as previously treated patients were included. Computerized national identity cards of all the patients were checked before inclusion in the study to confirm that they belong to North of Pakistan. Temporary residents or visiting patients from other parts of the country especially from Afghanistan were not included in the study. Patients having added Hepatitis B Virus (HBV), Hepatitis D Virus (HDV) and HIV infections were also excluded from the present study. All chronic HCV patients confirmed on 3rd Generation ELISA and further confirmed by Rotor Gene TM Real Time Quantitative PCR were analyzed for HCV Genotypes. Data were recorded in the form of tables and analyzed by using SPSS version 18. Statistical approach was applied using paired two samples t-test for means to check the difference among different groups of genotypes.

RESULTS

There are six main hepatitis C virus genotypes throughout the world. A study was designed to investigate the type of genotypes of hepatitis C virus present in patients of our study area, so for that purpose a total of 537 patients meeting the inclusion criteria, aged between 16 to 65 years, were included in this study in which 282 (53.1%) and 255 (46.9%) were males and females respectively (Figure 1).

In our study regarding HCV genotyping; 355 (66.11%) were type 3a, 14 (2.61%) 3b, 40 (7.45%) type 2a, 5 (0.93%) types 2b, 1a and 1b each, 9 (1.67%) patients mixed types 2a and 3b, 3 (0.56%)

Table 1: Numbers of different genotypes and their percentage in the sample of 537

S.No.	Genotypes	Percentage	Patients
1	3a	66.11	355
2	3b	2.61	14
3	2a	7.45	40
4	2b	0.93	05
5	1a	0.93	05
6	1b	0.93	05
7	2a+3b (mixed)	1.67	09
8	3a+3b (combined)	0.56	03
9	Un-type able	18.81	101

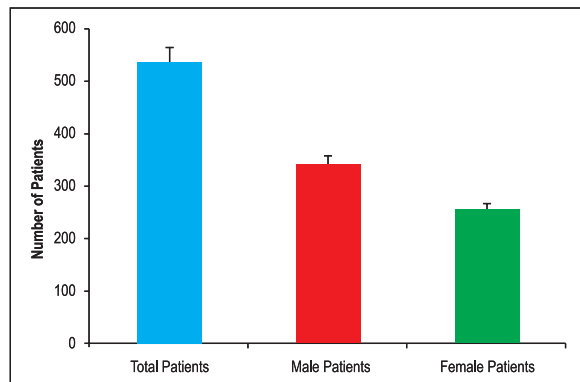


Figure 1: Gender Distribution of HCV Positive Patients (n=537).

were combined 3a and 3b and 101 (18.81%) were un-type able ($p < 0.05$). (Table 1)

DISCUSSION

Our study is the first of its type to determine HCV genotypes in the North of Pakistan. There was a higher proportion of male patients (53.1%) infected with HCV than females (46.9%). Previous studies in Pakistan also show similar higher prevalence in males (65%) as compare to females.^{9,10} This could be attributed to the more physical activities done by males in our community as compared to females thus experiencing greater risk of injuries, transfusions and hence exposure to the virus.

The most commonly isolated genotype was type 3 (68.72%) with 3a being 66.11% and 3b being 2.61%. Three patients (0.56%) had a combination of both 3a and 3b. Abbas et al⁹ also has reported genotype 3 to be present in 96% of the patient's studied. This prevalence (genotype 3 in 96% patients) is in contrast to that determined by another study carried

out in the South of Pakistan by Idress M et al showing 67.36% patients having infection with HCV genotype 3a¹⁰ but our results (68.72% genotype 3) are very close to this report. The second most commonly isolated HCV genotype in our sample population was type 2 (8.38%). This is in contrast to a study carried out previously by Abbas et al⁹ showing type 1 to be the second most common genotype with a prevalence of 11.5% all over Pakistan and 12.97% in Sindh.⁹ Another study carried out in Bahawalpur by Mansoor et al showed the same contrast with our study with type 3 being most common (71.4%) followed by type 1 (10.2%). Only 3.1% of the patients had type 2 HCV genotype. These results in our study population in the North of Pakistan are really encouraging because as compared to genotype 1, the genotype 2 is much more treatment responsive with better expected viral eradication rates with treatment.⁶⁻⁸

There is considerable regional variation in the distribution of various HCV genotypes with the neighboring countries. A study in the Northeast of Iran by Vossughinia et al reported genotype 3a (40%) to be the most common followed by 1a (39.2%). The almost equal ratio for the two types was followed by genotype 1b, 5 and 2.^{11,12} Abraham P¹³ also reported nearly similar results in India

Joukar et al¹⁴ showed that genotype 1a to be more common (59.4%) in chronic HCV patients undergoing regular hemodialysis in Iran as compared to 3a (40.6%) in the rest of the general population. On the other hand, Medhi S while studying the tribal dominated parts of the Northeast India reported an overall higher prevalence of genotype 4 (30.8%) while genotype 2a being the most common (28.6%) in patients with acute hepatitis.¹⁵ Another review study by Sievert et al¹⁶ showed genotype 1 to be the most common genotype in Australia and China, genotype 3 in Pakistan while genotype 4 to be most prevalent in the Middle Eastern countries. It is therefore evident that considerable variations in the distribution of HCV genotypes may occur in different countries as well as in different regions of the same country like various other studies from Pakistan for example Ahmad et al¹⁷ has reported in 2007 that 81% of individuals had genotype 3 while only 9.5% had genotype 1. Similarly Hakim et al¹⁸ reported in 2008 that 51% of HCV patients had genotype 3 while 24% had 3a/3b co-infection and 16% had genotype 3b. Afridi et al¹⁹ had stated that 50% of HCV patients had genotype 3a followed by 3b and 1a.

Knowing the particular distribution of various genotypes remain of paramount importance since the treatment modality, its duration as well as expected outcome depends on the particular genotype involved. When treated with a combination of Peg-Interferon and Ribavirin, the sustained virologi-

cal response (SVR) for type 2 and 3 is much higher (70-80%) as compared to those achieved with type 1 (45%).^{6-8,20-22}

The much lower prevalence (1.83%) of the harder to treat type 1 genotype in North of Pakistan gives rise to the possibility of giving an empirically smaller duration of antiviral treatment while expecting improved viral clearance rates. This vital piece of information can help to reduce treatment cost in patients purchasing the expensive antiviral drugs. This information remains of paramount importance for the treating clinicians working in parts of the province where the HCV genotypes determination facilities are not available.

CONCLUSION

We have reported for the first time the various HCV genotypes prevalent in the North of Pakistan. Seeing the preponderance of genotype 3a as the most prevalent in our study population, we recommend shorter courses of empirical treatments and expected better viral clearance rates. However, at places where the HCV genotypes determination facilities are available, the particular HCV genotypes involved in causing infection must be determined before starting treatment.

REFERENCES

1. Bosan A, Qureshi H, Mohamud KB, Ahmad I, Hafiz R. A review of hepatitis viral infections in Pakistan. J Pak Med Assoc 2010; 60:1045-58
2. WHO: Factsheets World Health Organization; 2009. Hepatitis C. Available from: <http://www.who.int/mediacentre/factsheets/fs164/en/index.html>
3. The 38th EASL Consensus Statement, The european association for the study of liver, July 2003.
4. Abbas SZ, Batool SA, Pathan I, Muhammad SR, Abbas SQ. Liver disease: admissions and mortality in medical ICU at a rural center in Pakistan. Pak J Med Sci 2007; 23:713-6.
5. World Health Organization. Unsafe injection practices having serious large-scale consequences. Press release WHO/14. Geneva: WHO, 2000:1-20.
6. Rumi MG, Aghemo A, Prati GM, et al. Randomized study of peginterferon-alpha 2a plus ribavirin vs. peginterferon-alpha2b plus ribavirin in chronic hepatitis C. Gastroenterology 2010; 138:108-15.
7. Ghany MG, Nelson DR, Strader DB, et al. An update on treatment of genotype 1 chronic hepatitis C virus infection: 2011 practice guideline by the American Association for the Study of Liver Diseases. Hepatology 2011; 54:1433-44.
8. Namazee N, Sali S, Asadi S, Shafiei M, Behnavab B, Alavian SM. Real response to therapy in chronic hepatitis C virus patients: A study from Iran. Hepat Mon 2012 ; 12:e6151.

9. Abbas SZ, Ali M, Muhammad AH, Shaw S, Abbas SQ. Frequency of HCV infection and its genotypes among patients attending a liver clinic and voluntary blood donors in a rural area of Pakistan. *Pak J Med Sci* 25; 4:579-82.
10. Idress M, Riazuddin S. Frequency distribution of hepatitis C virus genotypes in different geographic regions of Pakistan and their possible routes of transmission. *BMC Infect Dis* 2008; 8:69.
11. Masroor A, Qazi M, Fayyaz G, Chaudhary MD, Jamil A, et al. Hepatitis C virus genotypes in Bahawalpur. *Biomedica* 2006; 22:52-4.
12. Vossughinia H, Goshayeshi LA, Bayegi HR, Sima H, Kazemi A, et al. Prevalence of hepatitis C virus genotypes in Mashhad, Northeast Iran. *Iran J Public Health* 2012; 41:56-61.
13. Abraham P. Viral hepatitis in India. *Clin Lab Med* 2012; 32:159-74.
14. Joukar F, Khalesi AK, Jafarshad R, Rahimabadi MS, Mansour-Ghanaei F. Distribution of hepatitis C virus genotypes in haemodialysis patients of Guilan, Northern Islamic Republic of Iran. *East Mediterr Health J* 2012; 18:236-40.
15. Medhi S, Goswami B, Das AK, Singh TB, Husain SA, et al. New insights into hepatitis C virus infection in the tribal-dominant part of Northeast India. *Arch Virol* 2012; 157:2083-93.
16. Sievert W, Altraif I, Razavi HA, Abdo A, Ahmed EA, et al. A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt. *Liver Int* 2011; 2:61-80.
17. Ahmad N, Asgher M, Shafique M, Qureshi JA. An evidence of high prevalence of Hepatitis C virus in Faisalabad, Pakistan. *Saudi Med J* 2007; 28:390-5.
18. Hakim ST, Kazmi SU, Bagasra O. Seroprevalence of Hepatitis B and C genotypes among young apparently healthy females of Karachi-Pakistan. *Libyan J Med* 2008; 3:66-70.
19. Afridi S, Naeem M, Hussain A, Kakar N, Babar ME, Ahmad J. Prevalence of hepatitis C virus (HCV) genotypes in Balochistan. *Mol Biol Rep* 2009; 36:1511-4.
20. Jothimani D, Chandy GM, Conjeevaram H. A new era in the treatment of chronic hepatitis C infection. *Indian J Gastroenterol* 2013; 32:71-9.
21. Sarin SK, Kumar CK. Treatment of patients with genotype 3 chronic hepatitis C - current and future therapies. *Liver Int* 2012; 32:141-5.
22. Swain MG, Lai MY, Shiffman ML, et al. A sustained virologic response is durable in patients with chronic hepatitis C treated with peginterferon alfa-2a and ribavirin. *Gastroenterology* 2010; 139:1593-1601.

CONFLICT OF INTEREST
Authors declare no conflict of interest.
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None declared.