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Epidemiology of Hepatitis B Virus Genetic Diversity Vs and Diagnostic Molecular Markers of Hepatitis C Virus Core Gene

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ABSTRACT

Hepatitis B Vs in most cases appears to chronic liver inflammation and liver in the long term can lead to cirrhosis or cancer. Attempts have been made to treat and control the disease as a major health problem in the world and is considered done. Recent studies on the biology of the virus cause diagnostic markers including hepatitis B virus genotypes Vs and seeking nuclear gene has been mutated strains. On the other hand the distribution of genotypes of the virus in different countries and the relationship between genotype and different serotypes in the world. Determine the different types of hepatitis genotype should be determined in each country of the region, such as determining the therapeutic protocol to implement antiviral therapy based on genotype will be different. In this study published papers related to the prevalence of hepatitis B virus genotypes and cultivars Vs mutant genotypes were searched. The results show that in patients with hepatitis B genotype dominant form in Asia C In northern and central Europe genotype A, in the countries around the Mediterranean and East Europe genotype D in Latin America genotype H and F, Genotypes in Africa a and E In patients with genotype 1 Hepatitis C virus. Also, in the United States and northern Europe, genotype 2 in sub-Saharan Africa and Central and West Africa and South-East Asia, genotype 3 in sub-Saharan Africa and the Far East and the Indian subcontinent, genotype 4 in the Middle east and Africa, genotype 5 in south Africa and genotype 6 in south China and south east Asia are high. Cirrhosis of the liverin genotype 1 and 4 are more common.With the arrival of protease inhibitors of Hepatitis C virus in the field of treatment and drug resistance observed in these types of treatments, studied the genome of hepatitis C in the presence of mutations associated with resistance to protease inhibitors has become important. In hepatitis C from the marker gene polymorphisms I LB 28 and genotype, gene polymorphisms. ITPA to identify mutations associated with resistance to inhibitors are used.

Keywords: Hepatitis B Vs, genotype, epidemiology, molecular markers.

INTRODUCTION

Hepatitis 10 or 15 years ago were identified. Management of hepatitis viruses has changed since the early nineties. Today, the proliferation of hepatitis B and C can be a powerful anti-virus suppressed. Many new antiviral drugs, especially Protease polymerase inhibitors, are currently under development. Hepatitis B virus genotypes and response to treatment of chronic hepatitis C is one of the most important criteria are considered as well as the distribution of genotypes of the virus in certain communities is different.

Determine the distribution of different genotypes of hepatitis B Vs must be determined in each country of the region, such as determining the therapeutic protocol to implement antiviral therapy based on genotype will be different. Hepatitis C genotype by diagnostic markers including search and core genes can be mutated strains of hepatitis C genotype determined resistance to the drug. [2001.1, Simmonds *et al*]

Hepatitis B virus genotypes

10 genotypes of hepatitis B virus (A-J), various types of different serotypes (ayr, adw, adr ayw) Is the distribution of genotypes of the virus in different countries and the relationship between genotype and different serotypes in the world. [2, 2014 Pourkarim *et al*]

Epidemiology of hepatitis B virus

Worldwide prevalence of hepatitis B virus has a wide range. In 12% of the population, including West Europe, USA, Canada, Australia and New Zealand show a lower prevalence of hepatitis B virus. In these areas, Risk of infection is less than 20%. About 43 percent of the world population, including the Mediterranean countries, Japan, Central Asia, Middle East, South America and Latin shows the average prevalence of hepatitis B virus. In more than 60% of the world's population, South East Asia, China and sub-Saharan Africa shows a high prevalence of hepatitis B virus] Wasley *et al* [4, 1975, Stevens *et al* 3, 2008]. Iran Hepatitis B is an average areas booklet. In Iran, 35% of people with the virus have an average of 3% (approximately 2/000/000) are carriers of the virus, but the rate of prevalence in different provinces, for example, Sistan and Baluchestan differ by more than 5% arrives. In high prevalence areas where the standard of living is lower and where the socio-economic standard is lower, more disease have been reported. The difference in the prevalence of the disease in different parts of the world is probably age-related diseases. [Haghshenas *et al*, 2014, 5]

According to the vaccination of infants and high-risk individuals, the prevalence percentage (and number) diseases in the world has decreased. The prevalence of chronic hepatitis B In different parts of the world is different from the direction of the three Logic prevalence of high, medium and low yields are areas with low prevalence, including the US, Western Europe, Australia and New Zealand that 1 to 2 percent of the population are chronic carriers of hepatitis B Respectively. Areas with intermediate prevalence, including the countries of the Mediterranean area, Japan, India, Singapore, Middle East, South America and Latin 3 to 5 percent of the population carries hepatitis B Respectively. Regions with high style, Southeast Asia and Africa, 10 to 7% of the population are chronic carriers of hepatitis B Respectively.

Africa

African countries have the highest rates of hepatitis B virus. Research with several countries Including Ivory Coast, Ghana, Cameroon and Uganda took place showed high genetic diversity in the genotype of the virus. Prevailing in the country genotypes Genotype A and E have been reported. Genotype A With serotypes A1, A2 and A3 is that all serotypes A It is in these countries. Genotype E Have different serotypes, of which serotype ayw4 and adw2 the highest frequency among patients, respectively [6, 2013 Joseph *et al*].

Latin America

Latin American countries have average rates of infection are hepatitis B virus. Among the features of different Latin American countries, the genotype of the virus. Hepatitis B virus genotypes in Latin America, including Mexico Type H and in Central America of F is. Liver cancer is rare in Mexico, but the relationship between liver cancers with serotype Fb 1 has been found in Argentina. This shows the importance of ensuring that genetic and environmental factors in the development of liver disease associated with hepatitis B virus in Latin America., [Roman *et al*, 2014, 7]

Asia

Southeast and East Asia, with 25 percent of the world's population with the highest rates of infectious diseases. The prevalence of hepatitis B virus in a wide range of areas. Genotypes that appeared in this logic are: A, B, C, D. In Asian countries such as Korea, Japan, Taiwan and China often, chronic hepatitis B is transmitted from infected mothers to babies. The predominant genotype in South Korea C Is that the rate of mortality from liver diseases in this country is relatively high. [Hyun Bae *et al*, 2005, 8]

China, Asia's most populous country with the highest immigrant populations is therefore different genotypes of hepatitis B virus is distributed in this region. The most common genotypes, respectively. B and C High rates of genotype C in China due to rapid adaptation of the virus with the host environment. Liver disease caused by infection with genotypes C There were periods are more aggressive disease. [9, 2011, Chan]

Now Iran is among the areas with low prevalence. In 1980, the prevalence of hepatitis B in Iran about 3%, but in recent decades the prevalence significantly reduced where responsibility can be public awareness about risk factors, the vaccination of 1993 for all newborns and people with risk high, such as health care workers and use of disposable syringes named. The main route of transmission from mother to infant and injecting drug users is and 56-51 percent of Iranian patients with cirrhosis of HBsAg Are positive. Genotypes in Iran D And subtype ayw2 is dominant and approximately 80% of patients with chronic hepatitis B in Iran HBeAg Negative [Haghshenas *et al*, 2014, 5].

Europe

Genotype in North and Central Europe A While more common in the countries around the Mediterranean and East Europe, the genotype D Sunburn appear in patients with genotype G Germany, the Netherlands and Georgia were diagnosed. [Schaefer *et al*, 2007, 10][Van der Kuy e t al, 2011, 12] [Vieth *et al*, 2002, 11]

Hepatitis C Genotype

Based on the differences in the genome, hepatitis C virus genotypes and subtypes are different. Hepatitis C with genotype 6 (6 5-4-3-2-1) and more than 100 subtypes that genotypes 1 and 4 of its global expansion and genotypes 5 and 6 specific areas of the world are seen. Determine the different types of hepatitis genotype should be determined in each country of the region. When determining treatment protocols to implement antiviral therapy based on genotype will be different. Iran conducted studies in order to identify the genotype of each specific objective pursued and on certain groups of society often have done. 13, 2014, Gower *et al*]

Epidemiology of hepatitis

Hepatitis C prevalence in different parts of the world there is a wide range. In some countries such as Egypt prevalence (> 10%) [14, 2013, WHO]. In West Africa, the Pacific and its prevalence is significantly higher than North America and Europe. It is estimated that 2 to 5 million patients with hepatitis C virus exist in Europe. The prevalence of hepatitis C virus antibodies in healthy blood donors US (1/6%), Italy (1/15%), Germany (0/4%) and Scandinavia (0/23%) [15, Hatzakis *et al* 2011]. In Europe and the US have chronic hepatitis C, the most common cause of cirrhosis, liver diseases and hepatomegaly cell carcinoma is the most important reason for liver transplantation. 16, 2009, Vogel *et al*]

The rate of infection in Iran is about 1% of the population. Hepatitis C virus genotypes significant differences in nucleotide and amino acid sequences themselves, which leads to differences in biological activity and thus viral pathogenesis can be caused by any of these genotypes. Among the most important differences in the genotype are considered physicians is significant difference between treatment response in patients with genotype 1 compared with patients with genotype 3 is, as in treatment with a combination of interferon alpha Pegylated and sustained viral response ribavirin in patients with genotype 1 patients with genotype 3 between 40 and 50 and between 70 and 80 percent. The prevalence of hepatitis C virus genotypes vary according to geographic locations: genotype 1 hepatitis C worldwide, including developed areas like North America and Europe can be found. Hepatitis C virus genotype 2 virus has spread in Central and West Africa and South East Asia as well as some Western countries, while genotype 3 hepatitis C, mainly in the Far East and the Indian subcontinent has been found [17, 2004 Simmonds]. Meanwhile, figures genotype 4, 5 and 6 of hepatitis C. Native particular geographic areas are as follows: genotype 4 hepatitis C, mainly in Egypt and sub-Saharan Africa, genotype 5 Hepatitis C in South Africa, 2010, [Antaki *et al* 18], and hepatitis C genotype 6 is found in southern China and South East Asian countries there. [Mellor *et al*, 1995, 19] [Alter, 2007, 20]

Genotype 1

Genotype 1 is the most common type of hepatitis C worldwide, especially in the United States and Northern Europe, which is about 70 percent sufferer's hepatitis C Chronic in the world [Hnatyszyn *et al*, 2005, 21]. Genotype 1 is the most common type of hepatitis C worldwide, the predominant subtypes a 1 b 1. Subtypes b 1 is transmitted through blood.

In addition, genotype 1 ratio to treatment with interferon-alpha / ribavirin were resistant. Increase response rates stable emergence of viral drug resistance is a concern that may affect the result of new treatments. [Sarrazin *et al*, 2012, 22]

Genotype 2

Hepatitis C genotype 2 for sub-Saharan Africa and South East Asia, [Sulbaran *et al*, 2010, 23]. In some European countries such as the Netherlands and France 2 hepatitis C genotype is more prevalent among immigrant populations. [van de Laar *et al*, 2006, 24]

Genotype 3

Research in Africa represent different genotypes on the continent. In Central and West Africa genotype 2 and genotype 3 hepatitis C has been developed South Africa. Hepatitis C genotype 3 in the first was established in South Africa to the Far East and the Indian subcontinent immigrants then moved [Abid *et al*, 2000, 25]. The researchers found a significant association between genotype 3 hepatitis C fibrosis and progression of fibrosis by increasing the speed of getting there. These observations may have important implications for the management of patients infected with the genotype. Subtypes a 3 is found mainly among intravenous drug users. [Bochud *et al*, 2009, 26]

Genotype 4

Genotype 4 hepatitis C in the Middle East and Africa, is common in Egypt prevalence is extremely high, the prevalence of ultra-high causing an increasing incidence of hepatocellular carcinoma in Egypt, which is currently the second leading cause of cancer mortality cancer among men in this country. The genotypes resistant to existing treatments. [el-Zayadi *et al*, 2005, 27]

Genotype 5

40% of patients with hepatitis C genotype 5 in South Africa, but sporadic cases in four countries: France, Spain, Syria and Belgium have been found. [Antaki *et al*, 2010, 28]

Genotype 6

6 genotypes of hepatitis C in southern China and South-East Asia is limited, and sometimes among immigrants Native countries can be found. Among the countries with high prevalence of genotype 6 than other genotypes include Vietnam, Thailand, Laos. Patients with this genotype most responsive to treatment than genotypes 3 Mybashnd. myzan injecting drug users, but higher than genotype 1. [Pham *et al*, 2009, 29][Yan *et al*, 2009, 30][Pybus *et al* 2012, 31]

Hepatitis C diagnostic molecular markers

Recent studies on the biology of the virus, including genotypes of hepatitis C cause diagnostic markers, and search for the core gene is mutated strains. With the arrival of protease inhibitor drugs to treat hepatitis B virus into Vs and observed drug resistance to these therapies, the hepatitis B virus genome Vs investigated for the presence of mutations associated with resistance to protease inhibitors has become important.

Gene polymorphisms ILB 28

Gene ILB 28 protein gene IFN » 3 which has an important role in the innate immune response to Hepatitis C virus infection. In the intermediate genes ILB 28 ILA 28 Number of genetic polymorphisms that are the most important ones polymorphisms rs12979860 and rs8099917. In patients with the favorable genotype of these polymorphisms, ie, rs12979860 CC and rs8099917 TT rates of spontaneous viral clearance and response to interferon combination therapy containing a significant increase compared to unfavorable genotypes of these polymorphisms, ie, rs12979860 TT and rs8099917 GG. The effect of this polymorphism on spontaneous viral clearance and response to treatment in patients infected with genotype 1-infected patients has been demonstrated, but in genotype 3 is located in the cool of ambiguity. Finally, it can be concluded IL28B One of the most powerful predictor of treatment response in patients infected with genotype 1 prior to treatment is and now it can be used as a prognostic factor in the treatment of Hepatitis C virus. [Domagalski *et al*, 2013, 32] [Amol *et al*, 2013, 33]

Genotype, gene polymorphisms ITPA

Dual therapy with ribavirin and interferon in some patients with adverse events such as anemia. This condition is one of the most important factors lowering the dose of ribavirin and reduce to pass your feet of virus Will cost. One of the genetic factors influencing the use of ribavirin and interferon anemia, gene polymorphisms ITPA In particular polymorphism rs1127354 and rs7270101. Variants of these polymorphisms are associated with a decrease in protein activity ITPase As a result, resistance against anemia associated with ribavirin, respectively. Knowing the genotype of these polymorphisms are of anemia during treatment with ribavirin and for measures such as the use of erythropoietin predicted taken into account. [Aghemo *et al*, 2014, 34][Jyh Hwang *et al*, 2015, 35]

Resistance to protease inhibitors

In recent years, the supply of drugs, including protease inhibitors and Boceprevir and Telaprevir, hepatitis C treatment changed. While treatment with these drugs with a call lasting more virus than the usual treatment in combination with interferon-alpha pegylated and ribavirin is the use of these drugs may be associated with the emergence of variants resistant to the treatment of virus that use restrictions protease inhibitors is. Protease inhibitors inhibit serine protease encoded by genes NS 3 Virus replication of hepatitis C inhibit and if variants containing mutations of resistance to these drugs in the treatment chosen viral load increases and therapy needed to clear the virus will not be, the result could be over treatment sequence analysis NS 3 Hepatitis C in the presence of resistant variants to investigate and, if necessary, to better manage patient [Fatima *et al*, 2014, 36].

RESULT

The results show that in patients with hepatitis B genotype dominant form in Asia C In northern and Central Europe genotype A, in the countries around the Mediterranean and East Europe genotype D in Latin America genotype H and F, Genotypes in Africa A and E In patients with genotype 1 Hepatitis C virus. Also, in the United States and northern Europe, genotype 2 in sub-Saharan Africa and Central and West Africa and South East Asia, Far East genotype 3 in sub-Saharan Africa and the Indian subcontinent, genotype 4 in the Middle east and Africa, genotype 5 in south Africa and genotype 6 in south China and south east Asia are high. Cirrhosis of the liver in genotype 1 and 4 are more common. With the arrival of protease inhibitor drugs to treat hepatitis B virus into Vs and observed drug resistance to these therapies, investigate hepatitis C viral genome for the presence of mutations associated with resistance to protease inhibitors has become important. In hepatitis C from the marker gene polymorphisms IL28B and genotype, gene polymorphisms ITPA to identify mutations associated with resistance to inhibitors are used.

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