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Hepatitis B and hepatitis C viruses: a review of viral genomes, viral induced host immune responses and worldwide epidemiology

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وزارة التعليم العالي والبحث العلمي
كلية الحلة الجامعة الاهلية
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فيروسات التهاب الكبد B والتهاب الكبد C: مراجعة للجينومات الفيروسية والاستجابات المناعية المضيفة المستحثة بالفيروسات وعلم الأوبئة في جميع أنحاء العالم

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بسم الله الرحمن الرحيم

(يرفع الله الذين امنو منكم الذين اوتوا العلم درجات والله بماتعملون خبيرخبير)

صدق الله العضيم

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Dedication

To my support and the pure spring that will continue to narrate my veins... To my tree that does not wither... To the shadow in which I shelter at all times**... My father**

To the wellspring of tenderness and the water of life... To the symbol of love and the healing balm... To God's paradise on earth... To the secret of my success with her prayers**... My mother.**

To the pillars of love and heart beats **... My brothers and My sister.**

Who helped and helped and was intended God's face ...
Give the fruit of my efforts this
I dedicate this work

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I thank God Almighty first and foremost for the great grace that He has bestowed upon me, then I thank those who favored them. My beloved parents do not cease to me for all their efforts from the moment of my birth to these blessed moments. For everyone who advised me, guided me in preparing this research . And I especially thank the distinguished “Dr. Ruqaya Yahya Abd AL-Shaheed”, for helping me Supporting me and guiding me with advice, education, correction, and all that she did with me .

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Summary*:*

study included Hepatitis B and hepatitis C viruses (HCV) are frequently propagating blood borne pathogens in global community. Viral hepatitis is primarily associated with severe health complications, such as liver cirrhosis, hepatocellular carcinoma, hepatic fibrosis . A literature review was conducted on hepatitis B virus (HBV), HBV genome, genotypic distribution and global epidemiology of HBV, HCV, HCV genome, HCV and host immune responses, HCV genotypic distribution and global epidemiology. The valued information was subjected for review. HBV has strict tissue tropism to liver. The virus infecting hepatocytes produces large amount of hepatitis B surface antigen particles which lack the DNA. It has capability to integrate into host genome. It has been found that genotype C is most emerging genotype associated with more severe liver diseases (cirrhosis). The approximate prevalence rate of genotype C is 27.7% which represents a major threat to future generations. Approximately 8% of population is chronic carrier of HBV in developing countries. The chronic carrier rate of HBV is 2%-7% in Middle East, Eastern and Southern Europe, South America and Japan. Among HCV infected individuals, 15% usually have natural tendency to overcome acute viral infection, where as 85% of individuals were unable to control HCV infection. The internal ribosomal entry site contains highly conserved structures important for binding and appropriate positioning of viral genome inside the host cell. HCV infects only in 1%-10% of hepatocytes, but production of tumor necrosis factor alpha (from CD8+ cells) and interferon-gamma cause destruction of both infected cells and non-infected surrounding cells. Almost 11 genotypes and above 100 subtypes of HCV exists worldwide with different geographical distribution. Many efforts are still needed to minimize global burden of these infections. For the complete eradication of HBV (just like small pox and polio) via vaccination strategies, sincere efforts would be required from government and nongovernmental organizations.

الخلاصة :

شملت الدراسة فيروسات التهاب الكبد B والتهاب الكبد C (HCV) التي تنشر في كثير من الأحيان مسببات الأمراض المنقولة بالدم في المجتمع العالمي. ويرتبط التهاب الكبد الفيروسي في المقام الأول بمضاعفات صحية خطيرة، مثل تليف الكبد، وسرطان الخلايا الكبدية، والتليف الكبدي. تم إجراء مراجعة للأدبيات حول فيروس التهاب الكبد B (HBV)، وجينوم فيروس التهاب الكبد B، والتوزيع الوراثي وعلم الأوبئة العالمية لفيروس التهاب الكبد B، وفيروس التهاب الكبد الوبائي، وجينوم فيروس التهاب الكبد الوبائي، وفيروس التهاب الكبد الوبائي والاستجابات المناعية للمضيف، والتوزيع الوراثي لفيروس التهاب الكبد الوبائي وعلم الأوبئة العالمية. تم إخضاع المعلومات القيمة للمراجعة. يحتوي فيروس التهاب الكبد B على انتحاء أنسجة الكبد بشكل صارم. ينتج الفيروس الذي يصيب خلايا الكبد كمية كبيرة من جزيئات المستضد السطحي لالتهاب الكبد B والتي تفتقر إلى الحمض النووي. لديها القدرة على الاندماج في الجينوم المضيف. لقد وجد أن النمط الجيني C هو النمط الجيني الأكثر ظهوراً والمرتبط بأمراض الكبد الأكثر خطورة (تليف الكبد). يبلغ معدل الانتشار التقريبي للنمط الجيني C 27.7%، وهو ما يمثل تهديدًا كبيرًا للأجيال القادمة. ما يقرب من 8٪ من السكان هم حاملون مزمنون لفيروس التهاب الكبد الوبائي في البلدان النامية. معدل الناقل المزمن لفيروس التهاب الكبد B هو 2%-7% في الشرق الأوسط وشرق وجنوب أوروبا وأمريكا الجنوبية واليابان. من بين الأفراد المصابين بفيروس التهاب الكبد C، عادة ما يكون لدى 15% ميل طبيعي للتغلب على العدوى الفيروسية الحادة، في حين أن 85% من الأفراد غير قادرين على السيطرة على العدوى بفيروس التهاب الكبد C. يحتوي موقع دخول الريبوسوم الداخلي على هياكل محفوظة للغاية مهمة للربط وتحديد المواقع المناسبة للجينوم الفيروسي داخل الخلية المضيفة. يصيب فيروس التهاب الكبد C فقط 1%-10% من خلايا الكبد، ولكن إنتاج عامل نخر الورم ألفا (من خلايا CD8+) والإنترفيرون جاما يتسببان في تدمير كل من الخلايا المصابة والخلايا المحيطة غير المصابة. يوجد ما يقرب من 11 نمطًا وراثيًا وأكثر من 100 نوع فرعي من فيروس التهاب الكبد الوبائي (سي) في جميع أنحاء العالم مع توزيع جغرافي مختلف. ولا تزال هناك حاجة إلى بذل الكثير من الجهود لتقليل العبء العالمي لهذه العدوى. من أجل القضاء التام على فيروس التهاب الكبد B (تمامًا مثل الجدري وشلل الأطفال) من خلال استراتيجيات التطعيم، سيتطلب الأمر بذل جهود مخلصة من جانب المنظمات الحكومية وغير الحكومية.

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1-Introduction

Hepatitis B is life threatening liver disease caused by highly contagious blood borne viral pathogen known as hepatitis B virus (HBV). The HBV infection is one of the principle causes of severe liver disorders, including hepatocellular carcinoma, cirrhosis and end stage liver disease. In 1963, HBV was accidently discovered by Baruch Blumberg during his research on Australia antigen[1]. HBV is an enveloped virus which belongs to hepadnaviridae: with circular partially double stranded DNA representing highly compact organization. The HBV is smallest known DNA virus, having spherical shape with diameter of about 42 nm and genomic length of approximately 3.2 Kb[2,3]. The infectious virus particle, is responsible for causing infection in approximately five percent of world's population with 2 billion people infected with the virus and 350 million as carrier of chronic infection. The virus is responsible for 600 000 deaths each year.[4,5]

HBV has been recognized as an important global health problem. Tremendous efforts are being put forward by many scientists, from whole world, for prevention and control of viral infection. To date, successful vaccination strategies have been developed to arrest the viral spread among various populations [6] .The need of time is to put major emphasis on awareness about risk factors associated with transmission of hepatitis viral infection and to equip with adequate strategies for prevention of disease at national and international level. Hepatitis C virus (HCV) is blood borne pathogen which causes severe liver disorders, including hepatocellular carcinoma, hepatic steatosis, liver cirrhosis, end stage liver disease and various metabolic disorders. In 1989, HCV was identified by Choo et al. as a positive stranded RNA molecule related to Togaviridae or Flaviviridae .[7]

HCV has been classified into the genus hepacivirus of the family Flaviviridae. This virus is responsible for causing infection in three percent of world's population with approximately 170 million persons at risk of developing chronic hepatitis[8]. Due to continuous increase in number of viral infected hepatitis patients, World Health Organization (WHO) has recognized HCV as a major global health problem. Various epidemiological patterns and worldwide surveillance strategies are being performed for prevention and control of this disease. The HCV is small spherical enveloped virion with icosahedral capsid. The structure consists of an icosahedral lipid membrane with 2 glycoproteins (termed E1 and E2) that form heterodimers. An icosahedral nucleocapsid is thought to be present inside the viral membrane[9]. HCV can live on various environmental surfaces for more than sixteen hours and possibly up to four days.[10]

The Aim of study :

1-The study aimed to characterize hepatitis B and hepatitis C viruses (HCV) that frequently spread blood-borne pathogens in the global community.

2- Characterize the serious health complications that accompany viral hepatitis, such as cirrhosis, hepatocellular carcinoma, and cirrhosis.

3-The study included a review of the literature on hepatitis B virus (HBV), HBV genome, genetic distribution and global epidemiology of HBV, HBV, and HBV genome.

4-The study included host immune responses, genetic distribution of hepatitis C virus and global epidemiology.

2-Literature Review

2.1 .HBV and genome

The nucleocapsid of Dane particle is about 28 nm in size and constitutes hepatitis B core antigen. It is involved in packaging of viral genome. The hepatitis B surface antigen (HBsAg) present on the surface of HBV particle and 22 nm particles and tubular form, act as complex antigenic determinant. The infectious Dane particle acquires its membrane by budding or through secretory transport mechanisms via Golgi apparatus and endoplasmic reticulum. Membrane at outer envelope forms HBsAg which contains three viral surface proteins named according to their size of small, middle and large as HBsAg, HBmAg and HBlAg respectively. These proteins are encoded on same open reading frame (ORF) that encodes 3 start codons and get overlaps with polymerase ORF.[11]

The pregenomic RNA is the largest transcript which serves as template for viral replication. The only enzyme encoded by the viral genome, which reverse transcribes the pregenomic RNA, is viral polymerase and this enzyme is also located inside the nucleocapsid[12].

Some of the possible causes of persistent viral infection includes high viral load, high replication rate, viral inhibition of antigen presentation, viral mutations that antagonize antigen recognition, immunosuppressive effects of virus, immunologic tolerance, exhausted T cell response, insufficient co-stimulation of virus specific T-cells, inefficient viral presenting cells and alteration of T Helper Type 1 and T Helper Type 2 balance[20]. On average the incubation period of HBV is approximately 60-90 d. Among patients of clinical illness (jaundice), the prevalence of HBV is approximately less than 10% for the patients of less than 5 years but the prevalence rate ranges from 30%-50% for patients of 5 years or above. For HBV infection, the acute case-fatality rate is approximately in the range of 0.5%-1%. Generally the rate of chronic infection, among patients of less than 5 years of age, is 30%-90%. But the rate of chronic infection lies between 2%-10% for the patients of 5 years of age or more. The premature mortality rate from chronic liver disease is approximately 15%-25%[21].

The HBV has strict tissue tropism to the liver. The virus infected hepatocytes produces large amount of HBsAg particles which lack the DNA. The viral DNA is capable of integrating into host chromosome. Normally HBV is not cytopathic itself, instead in case of chronic hepatitis B disease, the liver damage takes place because of immune clearance phase of host against HBV infected hepatocytes.[22]

The primary liver carcinoma is considered as 5th most frequent cancer of world and hepatocellular carcinoma is the major type of primary liver carcinoma. In many areas of the world, more than 85% of hepatocellular carcinoma retains markers against hepatitis B and hepatitis C[23]. Two treatment options are available for the prophylaxis against HBV, which includes HBV and hepatitis B immune globin. For pre-exposure and post-exposure, hepatitis B vaccine is recommended. The vaccine is capable for long term protection against HBV infection. The hepatitis B immune globin can only provide temporary protection for approximately 3-6 months. This treatment option is usually recommended for post-exposure settings[24]. Hepatitis B viral form mutants are developed in some patients. These viral

mutants are resistant against one or more antiviral drugs. Researchers tend to develop novel antiviral therapeutic options in order to prevent resistance and minimize viral load.

2.2. HCV and genome

The size of HCV genome is 9.5 Kb. On both 5' and 3' termini of the genome there exists highly conserved untranslated regions, which flanks a large translational ORF (of approximately 9 000 nucleotides) capable of encoding polyprotein of 3 000 amino acids [9,25] .

A newly discovered protein which belongs to HCV is protein F, which is produced by ribosomal frame shift mutation around codon 11 of core protein. HCV infected individuals contains antibodies against this protein, so it is hypothesized that this protein usually expresses in those persons who are HCV infected. The information regarding function of protein F and how often it is expressed in infected individuals is unknown .[27]

A lot of information regarding HCV virion structure, binding mechanisms, functioning of viral proteins, release mechanisms and various host immune responses, is lacking due to the fact that HCV only infects humans and chimpanzees, and there is no reliable cell culture system or small animal model to facilitate complicated HCV research. Scientists are trying to develop subgenomic replicon systems and novel mice models with chimeric human livers. This approach would open new doors of scientific progress towards identification of most potent drug targets against HCV[30,31].

2 .3. HCV induced host immune response

HCV infection causes activation of host innate immune responses. Such responses usually take place after two days post infection, with increased involvement of interferon regulatory factors, protein kinase R and antiviral gene products, like interferon-inducible genes and immune transcription factors[27]. The innate immune response was observed in all individuals, regardless of whether they developed chronic infection or controlled the virus. Development of chronic infection suggests viral resistance to the innate immune responses, which probably exist due to interference of HCV proteins with pathways associated with innate immune system .

Among HCV infected individuals 15% had natural tendency to overcome acute viral infection, whereas 85% of individuals were unable to control HCV infection. The mystery behind this natural phenomenon is still unknown. However, among those who successfully control HCV infection, IFN-γ is preferentially expressed in liver (through T lymphocytes) several weeks post-infection. It results into expression of various chemokines which attract T cells and various proteins involved in antigen processing and presentation .[27]

Among those individuals who control viral infection, there is increase production of CD4+ and CD8+ T cells. The chronic viral infection occurs when individuals are unable to mount HCV-specific T cell responses. Another possible reason is influence of strong immune responses which initially cause RNA clearance, followed by contraction in CD8+/CD4+ level and ultimately results rebound in viremia[25,27,33]. According to Sun et al.[34], there exist

significant anomalies in immune response patterns among patients who exhibited viral clearance and those who were chronically infected with HCV. It includes, reduced frequency and limited capacity of HCV specific CD8+ cells, CD4+ cells with less production of interleukin-2 and impaired dendritic cells[34]. It has been reported that the T cell identifies dendritic cell via molecular signature at immunological synapse (a contact point). If the synapse signals for presence of foreign body, it would trigger T cell attack.[34]

Chronically infected HCV patients possess decreased frequency of natural killer (NK) T cells and impaired NK cell activity, this response get reversed in patients undergoing alpha-interferon therapy. These cells (NK and NKT cells) tend to alleviate pathogenic attack before activation of adaptive immune system. It is further supported by literature that these cells are responsible for activation of adaptive immune responses and regulation of autoimmune responses[33]. HCV cause infection only in 1-10% of hepatocytes, but production of IFN-γ and tumor necrosis factor alpha from CD8+ cells cause destruction of both infected cells and non-infected surrounding cells. Such high level of cell death and regeneration rate leads to onset of hepatocellular carcinoma[33]. The common treatment available for chronic HCV infected patients is combination therapy including pegylated alpha-interferon and the ribavirin which is a nucleoside analog. Usually it requires single injection per week .[35]

Although exact mechanism of action of these drugs is difficult to understand, yet it has been implicated that degradation of positive strand RNA and suppression of viral protein synthesis are principle mechanisms involved to arrest viral replication. It has been reported that this treatment option is only 50% effective against HCV genotype 1. And the efficacy for genotypes 2 and 3 was reported as 80%[30,36]. Unfortunately there is no alternative treatment for non-responders. Severe adverse reactions in response to interferon/ribavirin therapy usually drag doctors towards prescription of lower dose. One of the most sadden side effect of the aforementioned therapy is that combination therapy can worsen liver disease (with major symptom of viral infection) due to which only a subset of patients could get relief from HCV infection. There is an urgent need for identification of novel antiviral strategies and designing new drugs to combat lethal viral infection[36,37].

2.4 .Genotypic distribution of hepatitis B virus

Hepatitis B virus infection is distributed worldwide in the form of eight different genotypes (A-H)[38]. A newly described genotype I is also a pivot of interest for future researchers[39]. There exists at least 8% nucleotide sequence dissimilarity among eight known HBV genotypes. In Pakistan genotype D is most prevalent with estimated prevalence rate of 63.71%. This genotype is usually less responsive towards interferon therapy. The prevalence of genotype A, C, B in Pakistan is 10.036%, 7.550% and 5.335% respectively. The reported prevalence of mixed genotypes and untypable genotypes is 9.93% and 2.37% respectively[40]. According to the most recent study conducted by Awan et al. it has been reported that genotype C is most emerging genotype associated with more severe liver diseases (cirrhosis). The approximate prevalence rate of this genotype is 27.7% which represents a major threat to future generations.[41]

The genotype A is most prevalent in Africa, South East Asia including Philippines and Europe. It has two subtypes named as A1/Aa (most prevalent in Asia and Africa) and A2/Ae (most prevalent in Europe and United States). The genotypes B and C are most prevalent in Asia. The genotype B exist in two geographical locations named as B1/Bj (most prevalent in Japan) and B2/Ba (most prevalent in Asia) which is further classified into four distinct clades (B2-B4). The genotype C exit in two geographical locations named as C1/Cs (most prevalent in South-East Asia) and C2/Ce (most prevalent in East Asia) which is further classified into five distinct clades (C1 present in Myanmar, Thailand and Vietnam, C2 present in China, Korea and Japan, C3 present in New Caledonia and Polynesia, C4 present in Australia and C5 present in Philippines). The genotype D is most prevalent in India, Mediterranean and Middle East. It has been further classified into seven subtypes (D1-D7). The genotype F or H are mostly prevalent in Central and South America. The genotype F is further classified into four subtypes (F1-F4). The genotype G is most prevalent in France and Germany. It has been reported that genotypes A, D and F are most occurring in Brazil. In United States all genotypes exist with difference in frequencies based on ethnicity[42-45].

2.5. Genotypic distribution of HCV

HCV is increasingly recognized as major health care problem in the whole word. Despite of strenuous efforts from scientists, antiviral approaches could not completely eradicate it due to the fact that HCV is extremely heterogeneous. HCV is an RNA virus and lacks effective proofreading ability after its replication, that's why it introduces several mutations and keeps on evolution with respect to time. Mutations are not randomly distributed in the whole genome, instead these exist at hyper-variable regions of the genome which encode for envelop proteins; hence enable the virus to escape from host immune surveillance[46]. HCV has been categorized into various genotypes, having 67% nucleotide sequence identity of members with each other[47].

Up to date 11 genotypes and above 100 subtypes of HCV exists worldwide with different geographical distribution[48]. In Pakistan the most prevalent genotype is 3 followed by genotype 1 and 2[49]. Similarly genotype 3 and 1 are also foremost in Indian population[50]. According to P Simmonds et al., in United States of America and Canada, most prevalent genotypes are 1a, 1b, 2a, 2b and 3a. Similarly in South America, genotypes 1a, 1b, 2 and 3a are more common. In Northern Europe, genotypes 1a, 1b, 2b and 3a are more prevalent,, where as in Western Europe genotypes 1a, 1b, 2a, 2b and 3a are majorly distributed. In Southern Europe there is higher prevalence of genotypes 1b and 2c, whereas in Eastern Europe, genotype 1b is significantly distributed. In Africa, prevalence of genotype 4 is higher in parts Northern Central Africa; prevalence of genotype 4a is greater in Egypt; and prevalence of genotypes 1, 2, 3 and 5a is foremost in South Africa. In Pacific region, there is increased prevalence of genotypes 1a, 1b, 2a, 2b and 3a in Australia; in Taiwan genotypes 1b, 2a and 2b are more common; in Japan, there is an increased prevalence of genotypes 1a, 2a and 2b; in Hong Kong, genotypes 6a, 1b, 2a and 2b are highly distributed; in Thailand, genotypes 1b, 2, 3 and 6 are most prevalent; in Malaysia, genotypes 1b, 2 and 3 are mostly present; and in

Vietnam, there is an increased prevalence of genotypes 1b, 2 and 6. In Asia, prevalence of genotype 1b is higher in Turkey; prevalence of genotype 4 is greater in Middle East; and prevalence of genotypes 1b, 2a and 2b is higher in China[51,52].

2.6. Global epidemiology of HBV

The epidemiology of chronic HBV infection is distinct and diverse worldwide (Figure 3). Various seroprevalence studies conducted in different areas of world can easily be categorized into three distinct groups of higher, intermediate and lower endemicity[53]. In developing countries with larger population (South East Asia, Sub Sahara Africa, China, Indonesia, Nigeria and Amazon Basin), there is higher prevalence of endemicity with approximately 8% of population as chronic carrier of HBV. In aforementioned areas of world, 70% to 95% of population represents present or past serological markers against HBV. In another study, it has been reported that 60% of world population exist in high endemic zone of HBV infection[54-56].

Figure1 Global epidemiology of HBV and prevalence of HBV carriers.

The intermediate endemic zone of HBV infection, Middle East, Eastern and Southern Europe, South America and Japan exist. Among these populations the estimated infection is approximately 10-60% and the chronic carrier rate is 2-7%. In the region of intermediate endemicity, majority of infection develop in adults but rate of chronic infection are higher in infants due to early childhood exposure to viral infection[57]. The seroprevalence of HBV infection has been reported 5% in India, while in Italy, Russia and Turkey the prevalence rate ranges from 3%-10%[58-61].The HBV zone of lowest endemicity includes most developed countries such as Australia, North America and Northern and Western Europe. In aforementioned regions of world approximately 5-7% of population gets HBV infected with nearly 0.5% to 2.0% rate of chronic carriers. The most probable reasons of HBV infection in young adolescents could be exposure to high risk population groups, injection drug users, health care professionals, sex workers and unhealthy blood transfusion setups[62].

2 .7. Global epidemiology of HCV

Geographic distribution of HCV is not uniform (Figure 4). Several seroprevalence studies on different populations tend to describe the epidemiological patterns of disease. Although seroprevalence studies conducted on general population best describes the actual status of disease in that particular region, however majorities of such studies are conducted on high risk populations. Among various seroprevalence studies, majorities are based on cross sectional

design; however population based studies are better representative of entire community. Limited prevalence studies have been documented in various regions of world due to expenses and practical difficulties involved in detection of viral RNA in serum. Available data suggests that HCV is prevalent in 3% of world population[63]. The prevalence of HCV is considered highest in African and Asian regions, but countries with limited prevalence include Northern and Western Europe, Australia and North America[64]. China is world's most populous country with approximately 1 347 million population with estimated 38 million people infected with HCV[65,66]. India is second world's most populous country with estimated population of 1 210 million population which covers approximately 17.25% of world population. According to a community-based study conducted in West Bengal, the estimated prevalence of HCV was reported to be of 0.9% (Populous countries wiki; prevalence of HCV was reported to be of 0.9%)[65,67].

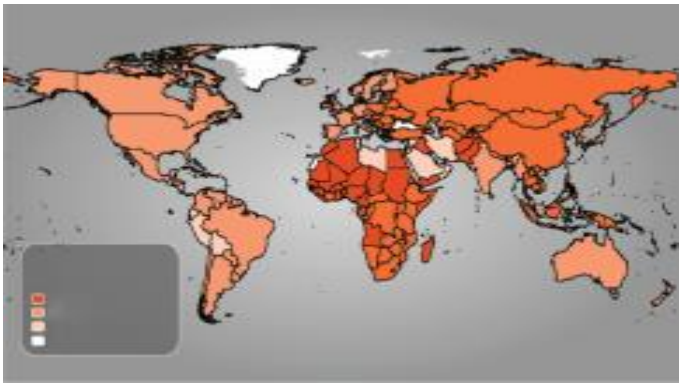

Figure 2. Global estimated prevalence of HCV.

United States of America is ranked as third world's most populous country with population of 313 million, which covers approximately 4.47% of world population. According to a study conducted on 21 214 nationally representative samples, the seroprevalence of HCV was reported as 1.8%[55,65]. Indonesia is ranked as fourth world most populous country with approximately 237 million people, which covers approximately 3.39% of world population. According to study conducted on 7 572 voluntary blood donors, the seroprevalence of HCV was reported as 2.1%[65,68]. Brazil is ranked as fifth world most populous country having population of 192 million people, covering 2.74% of world population. According to a study conducted on 66 414 voluntary blood donors, the estimated HCV prevalence was approximately 1.1%[65,69]. Pakistan is the sixth populous country of the world with approximate population of 179 million individuals covering 2.56% of world population. Khattak et al. conducted a study on 103 858 voluntary blood donors, it was reported that the seroprevalence of HCV was 4%[65,70]. Therefore on the basis of HCV infection prevalence in the six most populous nations in the world, Pakistan can be inferred as country with highest HCV prevalence among other most populous nations of the world. Viral hepatitis has been increasingly recognized as sever healthcare problem in world. This review provides comprehensive information regarding important HBV and HCV regions for conducting future

valuable research projects. A lot of efforts are required to completely eradicate HBV and HCV from this world like previous small pox viral pathogen which had been eradicated from world (decades ago) and polio virus which would be eradicated from world in near future. It is a well known fact that one in twelve people worldwide is infected with viral hepatitis. Due to its rampant proliferation, virus quasispecies and increased viral is associated mortalities. It is anticipated that hepatitis virus would soon emerge as most dangerous viral pathogen. HCV prevalence is unfortunately increasing day by day in developing countries due to limited awareness among general population. Up to date no HCV vaccine has been successfully prepared therefore a lot of efforts are still needed to reduce global burden of this disease. The most important way to prevent future burden of HCV is through knowledge and awareness via prevention strategies designed by public health specialists.

3.Conclusions :

the present study can conclude the following points:

1. Infection by HBV has a higher frequency in patients.

2. Hepatitis B virus reactivations was recorded in chronic cases.

3. Mono-genotypes in patients infected with HBV and genotype C were more prevalent. In addition to the existence of a relationship between viral load and genotyping.

4.The prevalence of HBV and HCV decreased steadily in blood donors during the past two decades. It should be asserted that most of the health policies and safety measures taken in recent years have been effective and promising.

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