

Review

Epidemiology of Hepatitis C Virus (HCV) Infection

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Hepatitis C virus remains a large health care burden to the world. Incidence rates across the world fluctuate and are difficult to calculate given the asymptomatic, often latent nature of the disease prior to clinical presentation. Prevalence rates across the world have changed as well with more countries aware of transfusion-related hepatitis C and more and more evidence supporting intravenous drug use as the leading risk factor of spread of the virus. This article reviews current hepatitis C virus prevalence and genotype data and examines the different risk factors associated with the virus.

Key words: Epidemiology, hepatitis C virus, blood transfusions, intravenous drug use

1. Prevalence

Hepatitis C virus (HCV) continues to be a major disease burden on the world. In 1999, the WHO estimated a worldwide prevalence of about 3% with the virus affecting 170 million people worldwide. [1] (*Table 1*). Generally, most studies of prevalence use blood donors to report the frequency of HCV usually by anti-HCV antibodies and do not report follow-up HCV testing. Using blood donors as a prevalence source may underestimate the real prevalence of the virus because donors are generally a highly selected population. [2]

In the Third National Health and Nutrition Examination Survey (NHANESIII) from 1988 to 1994, an estimated HCV prevalence of 3.9 million people was found in the United States (US) with 2.7 million people found to have chronic infection with HCV (positive HCV RNA). Neither sex nor racial-ethnic group was found to be independently correlated with HCV infection. However, a majority of patients that were HCV positive were below the age of 50. [2]

Among Central and South America, a recent community based study in San Juan, Puerto Rico, showed that estimated prevalence of HCV in 2001-2002 was 6.3%. [3] In Mexico, the prevalence reported was about 1.2%. (4) Among blood donors in Chile and Brazil, prevalence of HCV Ab was low - 0.3%, 1.14% respectively. [5,32]

In Europe, general prevalence of HCV is about 1% but varies among the different countries. [6] Prevalence of HCV antibody is 0.87% (1993-1994) in Belgium. [7] In the United Kingdom, at least 200,000 adults carry HCV. [8] In Northern Italy, prevalence of HCV Ab was 3.2%. [9] Three studies in Central and Southern Italy showed a higher rate of HCV (8.4%-22.4%), especially in the older population. [10-12] Among patients of general practitioners in Lyon, France, the prevalence of HCV was estimated to be 1.3%, very similar to the French general population. [13] Within the Russian army, frequency of anti-HCV was 1.5% among servicemen and donors with increased prevalence in the North Caucasus, Far East and Siberia (3.1-3.8%) compared to the Transbaikal region (0.7%). [14] Low rates were found in Hungary (0.73% of 15,864 blood donors.) [31]

Table 1: Hepatitis C estimated prevalence and number infected by WHO Region. Source: Weekly Epidemiological Record. N° 49, 10 December 1999, WHO.

WHO Region	Total Population (Millions)	Hepatitis C prevalence Rate %	Infected Population (Millions)	Number-of countries by WHO Region where data are not available
Africa	602	5.3	31.9	12
Americas	785	1.7	13.1	7
Eastern Mediterranean	466	4.6	21.3	7
Europe	858	1.03	8.9	19
South-East Asia	1 500	2.15	32.3	3
Western Pacific	1 600	3.9	62.2	11
Total	5 811	3.1	169.7	57

Recently, HCV prevalence studies have come out of Pakistan in the Middle East. 751 out of 16,400 patients (4.57%) were found to +HCV Ab from 1998-2002 with the largest age group from 41-50. [15] Among male blood donors in Karachi, Pakistan, the seroprevalence of HCV was 1.8% with a trend of increasing proportion of positive donors from 1998-2002. [16] There has been very high prevalence rates of HCV reported in Egypt in the past (28%). [17] This was confirmed among 90 blood donors in Cairo, where 14.4% were anti-HCV positive by RIBA test. [18] Then 26.6% among 188 blood donors and 22% among 163 donors were positive with both studies done in Cairo. [19, 20] Rates were lower in Saudi Arabia (1.8%) and Yemen (2.1%). [33, 34]

Intermediate rates of HCV have been reported out of Asia. From 1995-2000, 0.49% anti-HCV Ab were detected among 3,485,648 blood donors in Japan. [44] This was lower than the 0.98% of 10,905,489 blood donors reported in 1992. [21] In China, prevalence rates were generally low with rates around 1% among donors in Beijing and Wuhan. [22, 23] However, rates may be higher in certain areas such as the Hubei province (30.13%) and Inner Mongolia Autonomous Region (31.86%). [24] Low rates have been found in Malaysia (around 1.6%) and Singapore (0.54%). [25,26] Higher rates of HCV have been found in Thailand (3.2-5.6%). [27, 28] Within a smaller community of 103 residents in Sherpas, Nepal, only 1 person had a borderline reaction

in 2004. [29] In New Delhi, India, 1.85% of blood donors were positive. [30]

There have been fewer studies out of Africa, but lower rates have been reported - 1.6% among blood donors in Ethiopia and 0.9% in Kenya. [35, 36]

The estimated prevalence in Australia has been recently reported as 2.3% with the virus affecting 210,000 people by 2001. The 20-24 year old age group had the highest prevalence with strong majority of the infected population below the age of 50. [37]

2. Risk Factors

Intravenous drug use

Transmission of Hepatitis C virus has been strongly associated with intravenous and percutaneous drug and needle use. Reported cases of hepatitis C from intravenous drug use is on the rise in the US. In a study of injection drug users in Baltimore, Maryland from 1988 to 1996, 30.3% of participants developed anti-HCV antibodies with most in the first 2 years of the study. [38] Among 310 drug users in Antwerp and Limburg in Belgium, 71% and 46% had anti-HCV antibody, respectively. [39] The Hepatitis C European Network for C-operative Research (HENCORE) group reported a prevalence of hepatitis C of 80% among intravenous drug users (IVDU). [6] In the District Buner study in Pakistan, all 751 anti-HCV patients had a history of injections. [15] 90% of IVDU in Chang Rai, Thailand were positive for HCV. [27] 36.6% of randomly selected IVDU in Sydney, Australia and 74% of IVDU in Melbourne, Australia were HCV positive. [42,43] A recent study in London, England took 428 intravenous drug users below the age of 30 and found that 44% had antibodies to hepatitis C compared to 4% with HIV. This came out to an incidence of 41.8 cases per 100 person years of antibody to HCV. [40]

The importance of intravenous drug use can not be overemphasized. The prevalence of HCV among people who acquired HIV through intravenous drug use reaches 90%. [41] Co-infection of the two viruses can make treatment all the more difficult. Most countries with a young population of HCV infection must deal with intravenous drug use as the leading cause for spread of the virus. Many of these intravenous drug users do not know they are infected. Screening of HCV and treatment of substance abuse are extremely important in this group.

Blood Transfusions

Transfusion of blood products has been a leading cause of transmission of HCV; however, due to improved screening, transmission through transfusions has decreased in most developed countries. In Japan, incidence of post-transfusion non-A non-B hepatitis among those with less than 10 transfusions dropped from 4.9% (1988-Oct '89) to 1.9% (Nov'89-90) after screening with first-generation anti-HCV test was introduced. [45] In the US, incidence of post-transfusion hepatitis C dropped from 3.84% to 0.57% per patient (0.03% per unit blood) after HCV screening was introduced in 1990. [46] In England, the frequency HCV infected donations dropped from 1 in 520,000 (1993-98) to 1 in 30 million (1999-2001) when donations were tested for HCV RNA. [47]

However, incidence of transfusion related hepatitis C is still higher in other areas of the world. In a study of

147 Chilean patients with chronic hepatitis C, the most common risk factor was blood transfusion in 54% versus just 5% with IVDU. [48] A study was done in the largest blood bank in Santa Catarina, Brazil from 1991-2001 showing a significant drop in risk of acquiring HCV, but the lowest risk of 1:13721 was still almost 10 times higher than that of developed countries. [49] Despite better screening for selecting blood donors, there remains a need for some kind of HCV screening laboratory test.

Sexual activity

The role of sexual activity in the transmission of HCV remains unclear. In the NHANESIII study, number of sexual partners (OR 2.54 for 2-49 partners) and age at first sexual intercourse (OR 2.94) had significant correlation with HCV Ab and this has been confirmed in other studies. [2,3] Among 1257 non-IVDU in Baltimore at a STD clinic 9.7% were positive for HCV. [50] One hypothesis is that many of the hepatitis C patients may have injecting sexual partners. In one study, 15% of non IVDU women with an injecting partner had HCV. [51] More recently, a 10-year prospective follow-up study (8060 person-years) showed no evidence of sexual transmission among monogamous couples in Italy. [52] However, in a study among spouses in Egypt, it was estimated that wife to husband transmission was 34% and 10% among women with and without detectable HCV RNA. Husband to wife transmission was estimated at 3%. Overall, 6% were estimated to have contracted HCV from their spouse. [53] One must remember however that the prevalence of HCV is much higher in Egypt and this study did not emphasize monogamous relationships and transmission between spouses can only be assumed to be sexual in nature. Also recently, there was lack of evidence found for sexual transmission of HCV among men who have sex with men in the prospective ongoing Omega Cohort Study in the US (2653 person-years of follow-up). [54] All of this new evidence supports that sexual transmission of HCV is still rare but for some reason is higher among those with high-risk sexual activity.

Hemodialysis

It has been well documented that dialysis patients have a higher rate of HCV infection. In the 90's much of the world reported anti-HCV prevalence rates of 10-50% among hemodialysis patients with lower rates in such places as Ireland (1.7%). [55-60] Previously, rates in Europe were as high as 20-30%. [6] A more recent report from Saudi Arabia showed a prevalence rate of HCV among hemodialysis patients to be 9.24% compared to 0.30% among blood donors. [61] In a tertiary-care hospital in Mexico City, Mexico, the rate of anti-HCV was 6.7% compared to the roughly 1.2% prevalence in the population of Mexico. [62] The rate of seroconversion among hemodialysis patients with no other risk factors has been reported 1.38-1.9%/year. [63,64] These studies generally conclude that the transmission of the virus to hemodialysis patients is generally nosocomial with possible risk factors being failure to disinfect devices between patients, sharing of single-use vials for infusions, poor sterile technique, poor cleaning of dialysis machines, and poor distance between chairs. [65]

Special Populations

The prevalence of HCV has been noted to be higher in other populations as well. Among kidney transplants, the prevalence was reported to be as high as 33.3% in Italy with the frequency higher prior to 1990(50%) than after 1990 (27%). [66] Obviously, most of these kidney transplant patients underwent dialysis as well.

The United States Veteran Affairs medical centers have also reported a higher prevalence of HCV than the general population with percentages as high as 35% in the VA Palo Alto system. [67] The most recent study among 20 centers reported an estimated prevalence of 5.4% with 78% reporting a risk factor of either transfusion or intravenous drug use. Seropositivity was also associated with tattoo use and incarceration in this study. [68]

There is also an increased prevalence of HCV also among prison inmates. One example is the Riverside county jail system where 25% adults incarcerated carried the virus while only 2% of the juvenile detention population carried HCV. [69] The juvenile detention population therefore provides a target for teaching and intervention since many of these juveniles acquire the virus early in their adult years.

3. Genotypes of HCV

HCV is divided among six genotypes with numerous subtypes. These genotypes can differ up to 30% from each other in nucleotide sequence. Depending on the HCV genotype, length of treatment can differ. Genotype 1b is less responsive to alpha-interferon therapy compared to genotypes 2 and 3. It is therefore important to track the different genotypes of the HCV virus. In the NHANESIII study done in the US, 56.7% were classified as 1a, 17% as 1b, 3.5% as 2a, 11.4% as 2b, 7.4% as 3a, 0.9% as 4, 3.2% as type 6. [2] 50% of all infections were by genotype 1 with a higher percentage of genotype 3 among the IDU population in England. [70,71] Genotype 1b was the predominant genotype (46% among blood donors) in Chile and was found in all infected patients with hepatocarcinoma in one study. [5] This same genotype was also found in 82% of 147 chronic hepatitis C patients in Chile as well. [48] Genotype 1b is also dominant in Japan. [72-74] In Beijing, China, of 63 HCV-RNA samples, 52% were genotype 2 and 29% type 3. [22] In Thailand, HCV 3a was the most common genotype at 50-60% with 1a, 1b, and 6 comprising the rest (10-20% each). [27] Out of 90 patients in Estonia, 73.3% carried 1b, 20% with 3a, and 6.7% with 2a. [75] Genotype 3 is most common on the Indian subcontinent while genotype 4 is the most common genotype in Africa and the Middle East. [76-80] Genotype 5 can be found in South Africa and as mentioned above, genotype 6 can be found in south-east Asia. [81,82]

4. Prevention

Primary prevention of hepatitis C should target reduction of transmission of the virus. Prevention should target those at risk of acquiring the virus and should involve providing education, risk reduction counseling, HCV screening and substance abuse treatment. In the US, the Centers for Disease Control (CDC) suggest screening for the follow population:

- Persons who ever injected illegal drugs, including those who injected once or a few times many years ago.

- Persons who received a blood transfusion or organ transplant before July 1992.
- Persons who received clotting factor concentrates before 1987.
- Persons who were ever on long-term dialysis.
- Children born to HCV-positive women.
- Healthcare, emergency medical, and public safety workers after needlesticks, sharps, or mucosal exposures to HCV-positive blood.
- Persons with evidence of chronic liver disease.

Extra attention should be given to populations in specific settings such as correctional institutions, drug treatment programs, programs for high risk youth, HIV counseling and testing sites, and STD clinics. In these settings, physicians should always screen for intravenous drug use. Unlike HIV, HCV is found in high concentrations in filters, spoons, and rinsing liquids that may be used in association with needle drug use. Patients should be counseled on contaminated equipment being a source of infection. Addiction care and counseling should be focused on with possible referrals for psychotherapy and detoxification. [83-85]

Prevention in healthcare setting should also take place by having better sterilization, safer injections, reducing opportunities for percutaneous exposures to blood. In developing countries, better screening for donors and blood screening should take place to reduce the number of transfusion related transmissions.

Once a patient is found to have hepatitis C, that patient needs to be counseled to reduce the risk of HCV transmission to others. The physician should also offer counseling on treatment, reducing alcohol usage and immunization with hepatitis A, hepatitis B, pneumococcal and influenza vaccines. HCV negative persons with ongoing risk factors also require counseling and immunization with hepatitis A and hepatitis B vaccines. [83-85]

Future research in this field will need to be continued. We will need to continue to evaluate the incidence of the virus third world countries as well as the transmissibility of the various genotypes. Better prevention, screening and treatment methods for Hepatitis C virus all need to be elucidated.

Conflict of interest

The authors have declared that no conflict of interest exists.

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