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REVIEW ARTICLE

Hepatitis C virus infection: Epidemiology, risk factors and prevention strategies in public health in I.R. IRAN

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ABSTRACT

Hepatitis C is an emerging disease in the world and Iran. In this review the situation in Iran will be more clarified and the strategies for better control will be discussed.

Keywords: *Hepatitis C, Hemophilia, Thalassemia, Drug abuse, Harm reduction, Prevention*.
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INTRODUCTION

Hepatitis C virus (HCV) infection is a major cause of liver diseases related morbidity and mortality worldwide and represents a major public health problem (1-8). HCV can spread parentrally through both transfusion and contact with infected blood and its products, intravenous drug using, contamination during medical procedures and lack of attention to health precautions. Despite a declining incidence of new infections (9-11), the burden of disease, both in terms of mortality and in terms of cost, is expected to increase over the next decade and HCV infection will be a potential cause of morbidity and mortality and for the need of liver transplantation in the future. (12, 13). It is estimated that around 170-200 million individuals are living with HCV infection worldwide (14, 15). There are significant geographical variations in the prevalence of HCV infection in the world (1, 3). The incidence rate in western countries has decreased significantly (Due to efficient preventive strategies) (3) while it is still high in the developing countries (16) mainly as a consequence of the use of unscreened blood transfusions and unsafe parentral injections. Despite the fact that the risk of HCV transmission is supposed to be reduced due to the dramatic reduction of blood transfusion related transmissions but, the increasing proportion of infections is due to unsafe drug use injections (10, 17, 18). Control of HCV infection is an important issue in public health because the majority of infections does not resolve and lead to chronic disease (1, 19). Early detection, establishment of a surveillance system and risk factor evaluation and intervention in order to decrease the problem in the community can protect people from acquiring the infection.

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Risk factors

HCV is spread primarily by direct contact with human infected blood. High risks for HCV infection include intravenous and percutaneous

drug use, transfusion of blood products, hemodialysis and unprotected sex with multiple sex partners (20). The main risk factor for acquiring HCV infection before the routine anti-HCV screening of blood donors was blood transfusion (17, 21). After introduction of reliable tests for HCV screening in blood donors, the risk has decreased significantly in developed countries (22).

Today, intravenous drug abuse is the major cause for HCV infection (23). HCV has been identified as the most common viral infection affecting Intravenous Drug Users IDUs (24). Because of sharing contaminated needles and syringes, and other equipments used in injection, use of shooting galleries, cocaine use, unprotected sexual activities, and sharing the shaving equipments, IDUs constitute the most important groups at risk of being infected with HCV (17, 25) the latter being identified as the most common viral infection affecting IDUs (24-26). The prevalence rate of HCV in IDUs group is different in different parts of the world yet to control this infection in this high risk group as a strategy in the health system can help preventing the expansion of the infection to general population (16).

Unsafe injections by health care providers (57), unsterile shaving by barbers, tattooing and ear-piercing, known to be associated with HCV infection (58, 59), are common in developing countries. The sexual transmission of HCV infection is relatively rare but is possible, yet still important in heterosexual multipartners (27).

Modes of transmission in Iran

History of transfusion, undergoing endoscopy, non loyal sexual activities, non-intravenous (IV) drug abuse, IV drug abuse, and receiving wounds at war were found to be independent risk factors of being HCV-positive (17). And there are certain medical procedures, lifestyle patterns, and customs and cultural matters in Iran that predispose people to a number of HCV risk factors (17). No apparent risk factors could be demonstrated in around 20% of the positive cases (17). In a study in gypsies of Southwest of Iran, tattooing and phlebotomy were important risk factors for HCV infection (28, 29). The prisoners are a high risk group for HCV infection and more than 50% of intravenous drug abusers in prisons are anti-HCV positive (30) and also those who have history of tattooing and/or sexual contact inside the prison. The results indicated the importance of policies to prevent transmission of HCV infection during and following incarceration (31). The seroprevalence of HCV infection among drug abuser prisoners in comparison with the general population in Iran is very high (30% vs.0.2%) (32).

Injection drug users are the main pool for transmission of hepatitis C in our community. In addition to drug use, most drug abusers experience high-risk behaviors such as unsafe sex, tattooing , unsafe injections, improper disposal of hazardous waste, reusing used syringes without proper sterilization, sharing of needles by injection drug users are believed to facilitate the transmission of these infections, resulting in high prevalence rates in the country (5, 23, 33).

Epidemiology and prevalence of HCV infection in Iran

Unfortunately we had not overall and exact estimation of HCV infection in Iran and studies that were done on HCV prevalence are restricted to specific geographic locations, provinces and special groups. In a meta-analysis we found that the prevalence of HCV infection rate in Iran is 0.16% rendering the country to be considered as a low endemicity for HCV infection in general population. Blood donors are selected group and the prevalence rate in them is underestimated and the published data has shown that the prevalence of antibodies against HCV infection among blood

donors varies from 0.12% in Tehran (17), 0.5% in Babol (17) and 0.38-1.1% in Kashan (34).

Injecting drug use is the predominant mode of transmission in developing countries and the increasing rates among young people during recent years emerged a new health hazard for the community. Many studies in Iran are reported; the intravenous drug users (IDUs) had HCV infection between 38% and 46.6% (28, 31, 35).

Hepatitis C virus (HCV) infection is an important cause of morbidity and mortality in patients with hereditary bleeding disorders (36). Most of hemophiliac patients in developed countries have HCV infection and around 60%-90% have anti-HCV Ab (37, 38). This high prevalence is a consequence of higher survival rate of these patients. The prevalence of HCV infection in Iranian hemophiliacs is from 15.6% in Fars (39), a southern district of Iran, to 76.7% in North-West of Iran (40, 41). This heterogeneity in the prevalence of HCV infection mandate us for doing systematic review and we found that prevalence rate of anti-HCV Ab by Elisa in Iranian hemophiliacs is 40.836% (between 31.08 and 50.59) (Alavian et al 2009 In Press).

Hepatitis C virus (HCV) infection is one of the most important problems in transfusion-dependent patients, particularly for those who were transfused before HCV tests became available (42). The prevalence of HCV infection in Iranian thalassemia patients is from 15.7 to 63.8 percent (43, 44). HCV seropositivity was significantly associated with longer history of transfusion, but patients who had received their first blood transfusion after implementation of compulsory blood donors screening in Iran since 1995, had a significantly lower rate of HCV infection compared to those transfused before then (10). For better clarifying the prevalence rate of HCV infection in Iranian thalassemia patients, we did a systematic review and we found that the prevalence rate in 14 provinces in Iran is 15.765% (between 12.60 and 18.92%) (Alavian et al 2009 In Press).

Hemodialysis (HD) patients have a high HCV prevalence (45-48). The prevalence varies considerably among different countries and different centers in different cities (49). The prevalence rate of HCV infection in hemodialysis patients has decreased during recent years (11), but still remains a significant public health concern. Blood transfusion (47, 50, 51), hospitalization, and nosocomial patient-to-patient transmission (46, 49, 52) and impairment of cellular immunity are the main risk factors for acquiring the infection (53, 54). The prevalence rate of HCV infection in Iranian hemodialysis patients widely varies from 5.5% to over 24% in different provinces (49,55,56). For real estimation of HCV infection in hemodialysis patients we did a systematic review and we found that 13.57% of them were infected (Alavian 2009-Unpublished data). Our country is among the countries with lowest prevalence of HCV in hemodialysis patients in the Eastern Mediterranean Region. It seems that the prevalence rate of HCV infection in hemodialysis patients has decreased from many years before (11). In Iran, screening of blood donors for anti-HCV antibody started from 1996. In previous reports, blood transfusion was a risk factor for HCV transmission in Iranian HD patients (49, 57). Nowadays, blood transfusion does not seem to be a proven risk factor of HCV transmission in Iranian HD patients (58). Nosocomial transmission of hepatitis C in HD patients is common in some countries (59). Increased number of patients under treatment per unit, patients attending more than one treatment unit, contact with hepatitis B virus, type of dialysis equipment used and their sterilization and the duration of hemodialysis treatment are presented as more important nosocomial transmission risk factors for HCV infection (60, 61). Some studies reported cross infection through dialysis machines may be responsible for HCV infection in our

country (62). It seems that more attention in prevention program is needed for sterilization and control of infection in hemodialysis units. Prevention programs which have been started in Iran for evaluation and decrease of HCV infection rate in Iranian HD patients, had three main parts. The first part is to diagnosis all hemodialysis patients that are infected with HCV and to treat them even those who had kidney transplantation (63, 64). The second part is education of all nurses and health providers of dialysis centers for HCV infection and transmission routes (65). The last part is the organization of prevention program and planning them according to natural characters of each Iranian province (64). Iranian preventive program are aimed to reduce HCV infection in Iranian hemodialysis patients. Successful control of infection requires further studies to assess the effectiveness of different preventive policies (64).

Prevention Strategies

To prevent the spread of HCV infection assessing the risk factors of epidemiological characteristics, including modes of transmission is necessary. Who is at risk? Before answering this question, we should review the main risk factors for acquiring hepatitis C that are different in different communities. The risk factors can be identified in more than 90% of cases and in less than 10-20% the risk factors are unknown (66). The primary sources of HCV transmission are HCV-infected blood or blood products. Persons should be tested if they received a blood or blood component transfusion or organ transplant before 1995 in Iran, when sensitive tests were first used to screen donors for HCV antibodies in Iran (17). We should focus on war injured persons (Janbazan)(32, 67). In most parts of the world, injection drug use is the chief mode of transmission, and anyone who has ever injected illicit drugs should be tested (1, 66, 68, 69). Blood transfusion was a major risk for infection in the past. The estimated residual risk is low. Multiple transfused patients including those with thalassemia or hemophilia; have been at particularly high risk of developing hepatitis C. The high prevalence of anti-HCV antibody in hemophiliacs (from 30% to 100%) is due to the past exposure to untreated concentrates (44, 70-74). The majority of patients who acquire hepatitis C from injection drug use develop the chronic type of the infection and preventing transmission of hepatitis C among drug abuser is a critically important step. Unfortunately most young people are unaware of the risk of acquiring these infections from drug use. Needle exchange programs have been shown in some studies to reduce the risk of infection. Drug treatment programs and intensive community-based education programs will remain the mainstays of HCV prevention (75).

There is powerful evidence to support that imprisonment and sharing of syringe in prison are important risk factors for HCV infection (25, 69, 76-78). Injecting drug use and syringe sharing in prisons are common among IDUs (76, 89-81). In prisons, syringes tend to be used by many individuals. Thus, the risk of syringe contamination by these viruses is much higher in prisons than outside where syringes are usually shared with only one or two other peoples (79). In most prisons, it is not possible to entirely prevent the injection use of illicit drugs. The lack of access to new injecting equipment in the majority of prisons results in prisons effectively acting as an incubator for the hepatitis C epidemic. However, injection with contaminated equipment could be substantially reduced if sterile injection equipment is available. Against the general believe pilot studies which provided sterile injection equipment in prisons (via syringe vending machines) showed no any adverse effects such as increased injecting drug use or offences against prison personnel (25). The good opportunities in prison to contact large number of IDUs over longer periods should not be

missed. There should be specific activities to repeatedly counsel imprisoned IDUs on the risks of parenterally transmitted infections.

A range of preventive measures for IDUs has been implemented including syringe exchange programs, syringe vending machines, increased outreach efforts, and access to methadone maintenance treatment (MMT). Many studies have shown the lower levels of current syringe sharing among IDUs on MMT (82, 83). Other risk factors such as tattooing in prisons are important in transmission of HCV infection (76, 77, 84, 85). Educating prisoners about this important potential route for transmission of HCV is important and every tattooing in prison should be followed for testing. Syringe exchange and distribution is the primary HCV prevention strategy targeting IDUs, although evidence of risk reduction impact is stronger for HIV (86, 87) and there is only modest evidence of impact regarding HCV (83, 88, 89). High efficient transmission of HCV infection and the potential for transmission via contaminated injecting equipments other than needles and syringes, such as filters and spoons are the cause behind this difference (90-92).

Despite the growing evidence that hepatitis C is an urgent public health issue, few countries have developed strategic national responses to address the hepatitis C epidemics within their populations. Since people who inject or have injected illicit drugs are the main group infected in almost all local epidemics (24), hepatitis C responses, where they do exist, have largely focused on harm reduction. Although significant advances have been made in preventing HIV infection amongst IDUs with harm reduction programs, both prevalence and incidence of hepatitis C remains high amongst IDUs (93-95).

The data from some cross-sectional studies in IDUs, case control studies in blood donors or population-base studies would clarify the importance of IDUs as the main cause of hepatitis C in our region. We need a surveillance system to follow the prevalence and incidence of infection in IDUs in our region. The inability of any country, even those with established national hepatitis C policies, to prevent large numbers of new infections, has led some to question the effectiveness of harm reduction in relation to hepatitis C prevention (96). Other risk factors consist of sexual transmission in multiple sexual partners, commercial tattooing and body and ear piercing in developing countries (16, 97, 98). More control of places for these services may play an effective role in preventing the expansion of the disease in the community.

Screening patients with Hemophilia and Thalassemia for HCV infection and treatment of all patients for secondary prevention is recommended. The establishment of surveillance system for theses special patients is mandatory. HCV infection has negative impact on life expectancy in hemodialysis patients (64) and it should be controlled. Several prophylactic measures (49, 52, 99), have been suggested to avoid infection by HCV in the hemodialysis environment that consist of : screening patients with hemodialysis, ideally prescribing more erythropoietin to replace transfusion, routine dedication of hemodialysis devices is not recommended, carefully monitoring the infection control practices such as preparing medications in a separated area, cleaning and disinfecting dialysis station surfaces, washing hands and changing gloves between patient contacts, and items should be dedicated for use only with a single patient. New infection is evidently more frequent at centers that had a failure in infection control measures (49). Integration of surveillance system for early detection and discover the cause of acquiring the new infection and design a new strategy for prevention in future in the center is recommended and treatment of all patients (without contraindication) with Conventional or Pegylated interferon alone as soon as possible is a good strategy (100). With the decrease in the

prevalence rate of HCV infection in a center, the incidence rate will be decreased more and the cycle of transmission can be stopped! New infection is evidently more frequent at centers that had higher anti-HCV antibody prevalence and failure in infection control measures. Health care professionals especially hemodialysis nurses should be educated regarding the strict adherence to universal precautions. Finally the Ministry of Health and Medical Education should provide more facilities for early transplantation for hemodialysis patients

Conclusion

The epidemiology and prevalence of HCV infection has changed in many countries in the world including Iran (101). It is mandatory to pay more attention to new risk factors and act to prevent them as an important move for the control of the infection. Harm reduction as the core activity of triangular clinics serves the infected ones well while other supportive services help healthy but at risk population prevent the spread of HIV, HCV and other related ailments. We hope the already-in-place program of harm reduction becomes a nationwide practice to cover all high-risk populations including IDUs in and out of prison (102). We need better strategies to control hepatitis C in IV drug abusers (IVDs) in our community (103). Continued education of the public and healthcare professionals will play an important part in the control of this problem since injections in the healthcare setting are reported to be a risk factor for acquisition of hepatitis C in the community. We hope for a better future without new infected case with HCV.

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