

**Review article**

**Hepatitis C infection: a review on epidemiology and management of occupational exposure in health care workers for general physicians working in Iranian health network setting**

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**Abstract**

Hepatitis C virus (HCV) infection is a major public health in Iran as well as throughout the world. Health care workers (HCW) are occupationally at the risk of HCV infection. The aim of this article is to review the information about the epidemiology, nosocomial epidemiology, natural history, immunopathogenesis, and occupational risks associated with managing HCV in the health care workplace. Information obtained from previous investigation on HCV infection has yielded a better knowledge about HCV. Because data demonstrating the efficacy of any intervention are not yet available, no definitive post exposure anti viral therapy can be recommended for HCWs who are occupationally exposed to HCV. Based on existing data, the preemptive therapy and watchful waiting strategies outlined in this review article represent reasonable interim approaches to this complex problem.

**Keywords:** Hepatitis C virus; Occupational exposure; Health care workers

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## Introduction

Hepatitis C infection is a major public health in Iran as well as throughout the world [1-3]. The past two decades have been associated with the characterization of hepatitis C virus (HCV) as the major cause of hepatitis other than hepatitis B, introducing the effective screening tests for HCV detection to improve the safety of the blood supply, definition of the community and nosocomial infection of HCV, understanding the factors that influence on the transmission of HCV infection in the community, development of knowledge about the natural history of HCV infection, host immunological responses, and immunopathogenesis of diseases associated with chronic infection, liver cancer, and substantial progress in the development of therapeutic interventions to modify or cure HCV infection [4,5].

According to the epidemiology, routes of transmission, and prevalence of HCV infection in the community specially in high risk population such as intravenous drug users, prisoners and HIV positive persons, attending of the health care unites [3], this blood-borne virus represents a substantial risk to health care workers from occupational exposure to blood and other body fluids containing the virus in the workplace [6-9].

The aim of this article is to review the information about the HCV prevalence in communities and in special hosts, occupational exposure, natural history, pathogenesis, and occupational risks associated with managing HCV in the health care workplace. A systematic review of the literature on the epidemiology of hepatitis C from 1991 to 2010 using computerized bibliographic databases which include Pub Med, Current Content, Scopus, Embase and Iranmedex was made to find better understanding about HCV transmission in health care setting.

## Primary health centre

The Primary Health Centre (PHC) is the basic structural and functional unit of the public health services in Iran. PHCs were established to provide accessible, affordable and available primary health care to people [10]. Iran has been able to extend public health preventive services through the establishment of an extensive Primary Health Care Network including “Khanehe Behdasht”, urban/rural health centers and tertiary hospitals [10].

The Iranian health system has been established to meet healthcare needs identified through population health status surveys. Since 1984, the health system has become highly organized and efficient, resulting in a dramatic decrease in the common and endemic infectious diseases incidence and prevalence rate [11].

## Route of transmission

The hepatitis C virus is an RNA virus that is a major cause of chronic hepatitis and liver cancer [4]. It is transmitted chiefly through parenteral exposure to infected blood transfusions or injections with dirty needles [2]. Persons at highest risk for development of hepatitis C are injection-drug users [2,12-14], people who use cocaine with shared straws, and health care workers who are at risk for needle-stick and other exposures [1].

The risk of HCV transmission by a deep hollow needle injury from an HCV antibody positive source is about 10% but, if the source is PCR negative, this risk is 1.8% [5]. In overall, HCV transmission to Health care workers (HCWs) approximately occurs after 1% - 2% of needle sticks from HCV positive patients. Studies show that the risk of HCV transmission is 3%, between that of HIV (0.3%) and hepatitis B virus (HBV) (30%) [5]. Although the main route of transmission is via contaminated blood, curiously enough in up to 50% of the

cases no recognizable transmission factor/route could be identified. Therefore, a number of other routes of transmission such as sexual or household exposure to infected contacts have been investigated with conflicting results. Hepatitis C infection is an important public health issue globally. Better understanding of routes of transmission will help to combat the spread of disease.

Mother-to-child HCV transmission rate is 5%, but, when the mother is HIV co-infected this rate is higher. This risk increases with higher maternal viral load. Breast feeding does not transmit HCV to infant [15]. HCV transmission is not under influence of mode of delivery. HCV infection is not a contraindication for pregnancy, so HCV is not a routine screening test in pregnant women [16].

### **Transmission of HCV in the health care units**

#### *Patient-to-HCW transmission*

Hepatitis C is a blood-borne infection that is transmitted via transfusion or needle stick. By this reason, the health care workers are occupationally at the risk for HCV transmission from infected patients. Percutaneous exposure to blood is the primary mode of transmission for HCV from patients to health staff [6-9]. Splashes of blood from infected patients to HCWs' mucous membranes are reported to be a route of transmission for HCV [16,17].

#### *Patient-to-patient transmission*

Transmission of HCV in health care setting deserves special emphasis. Nosocomial transmission of HCV among patients and staff is described in the past reports from various countries. Hemodialysis settings, cardiovascular departments, endoscopic clinics [18] and orthopedic wards are hospital divisions that HCV transmission

has been reported. An increasing number of instances of nosocomial, patient-to-patient spread of infection as well as outbreaks of infection not linked to transfusion have been reported [19-24].

Spread in these units has been suggested to be due to environmental contamination, contaminated dialysis machines and inadequate infection control procedures in the dialysis unit [19]. In addition, patient-to-patient transmission in health care settings, primarily related to faulty injection practices, appears to be a reasonably important mode of HCV transmission in developing countries [25].

#### *HCW-to-patient transmission*

To date, iatrogenic transmission of HCV from HCV-infected HCW to their patients has been uncommon. The first report of documented iatrogenic transmission in surgery was reported from Spain [26].

### **Natural history**

Within days of exposure, often 1 to 4 weeks before liver enzyme levels raise HCV RNA can be detected in plasma [5]. The fact that two decades after identification of the etiologic agent the natural history of the disease remains remarkably clouded relates directly to the complexity of hepatitis C infection. More than 75% of hepatitis C infections do not cause jaundice and are asymptomatic; that is they are not detectable as significant clinical illnesses [27]. Acute, symptomatic hepatitis C infection is a relatively uncommon presentation (unlike hepatitis B virus infection). Up to 85% of individuals with positive anti HCV antibody test progress to develop chronic infection.

Individuals infected with HCV may clear their infection by their natural or cellular immune mechanisms, so they never develop productive HCV infection, and never produce antibody against HCV [28].

This population is usually missed by either HCV antibody testing or PCR for HCV RNA.

### **Immunity and pathogenesis**

Outcome of HCV infection is under influence of many factors such as genetics, host defense, environment, and the virus [5]. Both autoimmunity [29] and cryoglobulinemia [30] are frequently associated with HCV infection. Investigators have documented that cell-mediated immunity (CD8<sup>+</sup>) plays a significant role in the pathology of HCV infection as well as for the killing of HCV-infected hepatic cells [29].

HCV-associated extrahepatic manifestations such as porphyria cutanea tarda, lichen planus, vitiligo, cryoglobulinemia, membranoproliferative glomerulonephritis, lymphoproliferative disorders, a Sjogren-like syndrome, ischemic retinopathy, Systemic Lupus Erythematosus, and autoimmune thrombocytopenia are strong evidence for immune participation in the pathogenesis of HCV infection [30-32].

### **Humoral immunity**

Only 15% of HCV infected individuals; spontaneously clear hepatitis C infection, these phenomena are frequently associated with the development of specific antibodies directed against HCV. The fact that HCV infection persists in the face of the antibody response indicates that, in the chronically infected patients, antibody is insufficient to clear the infection. With respect to HCV infection, humoral immunity can assist in the direct neutralization of cell-free virions but can only play an extremely limited role in eradicating HCV inside cells [5].

### **Cellular immunity**

Both helper and cytotoxicity responses play important roles in host defense against HCV

infection. Previous studies demonstrate that T-helper and T-cytotoxic responses are both associated with resolution of HCV infection [33,34].

### **Prevalence of HCV infection**

Hepatitis C virus is a major cause of chronic liver disease in the world. The WHO estimates that 3% (170 million) of the world's population are chronically infected with HCV [35]. Epidemiology of HCV in Iran is affected by various factors such as geographical situation, mass immigration from Afghanistan, frequent travels to Turkey and Iraq, and illegal drug traffic from Pakistan and Afghanistan. It seems that the prevalence of HCV in Iran is less than 1% that is lower than that of other countries in the region: 1.1% in Yemen, 1.8% in Saudi Arabia, and 3% in Pakistan [2,36].

### **Clinical presentation**

Clinical presentation and outcomes of chronic hepatitis C is dependent on host factors that affect on the severity and rapidity of progression of the disease. The most important factors for acceleration of progression of cirrhosis are age at infection, alcohol abuse and diabetes with insulin resistance, obesity, fatty liver, HIV and/or HBV and/or HDV Co-infection [37,38].

### **Prevention of occupational transmission management of health care workers after exposure**

#### *Immediate management and follow-up strategies*

To give first aid to a person after an occupational exposure is important. Washing the puncture or open wounds with soap and water is the most useful intervention. In some papers sterile saline had been used for flushing the open wounds [39]. Rinsing with water is recommended for managing the splash exposures of the

mouth and nose. Flushing the eye with water or fluid designed for eye irrigation should be employed for splash exposures of the eyes.

Currently, the following approach is recommended for occupational exposures to HCV follow-up in health care workers: HCV-antibody testing of the source patient, HCV-antibody testing the exposed health care worker after exposure and at six months later and for alanine aminotransferase levels, testing supplementary HCV antibody tests to confirm the presence of HCV antibody; no post exposure immunoglobulin prophylaxis and antiviral agents, or immunomodulators; and health educating the exposed person about the risk of HCV infection, nosocomial transmission, and about strategies effective in preventing transmission of blood-borne pathogens, including hepatitis C virus in occupational settings [39].

Prophylaxis with immunoglobulin in contrast to hepatitis B infection, is not useful in managing occupational exposures to hepatitis C [39]. In individuals with occupational exposure to HCV immunomodulators are not recommended for prophylaxis [39]. In one report this approach was not successful in preventing infection [40].

### **Antiviral therapy**

Up now, no antiviral drugs other than alpha interferon are recommended for the treatment, or prophylaxis of HCV [5]. Preemptive therapy and watchful waiting both are reasonable approaches for HCV exposure management based on the currently available data. Monitoring the HCV viremia by PCR, measuring the alanine aminotransferase levels, and then making the decision to intervene are appropriate approaches to post exposure

management instead of the 3 to 6-month antibody testing recommended previously for these exposures [39,41].

The aim of the follow up is to detect acute hepatitis C so that appropriate management can be instituted [5]. The HCW should be informed of the risk of transmission to secondary contacts, especially during the first six months following the incident. During this period the HCW should be advised: 1- not to donate plasma, blood, body tissue, breast milk or sperm; 2- to consider safe sex (e.g., use of condoms) during menstruation or if there is genital ulceration, but there is little evidence that HCV is sexually transmitted to a significant degree; 3- to seek expert medical advice regarding pregnancy and/or breastfeeding; 4- to seek expert clinical advice regarding the need to modify work practices involving exposure prone procedures (in the case of highest risk percutaneous exposures) and 5- to seek expert clinical advice and work practices modification in exposures developing clinical or serological evidence of HCV.

HCW with evidence of acute hepatitis should be referred to a specialist experienced in the management of hepatitis. If the risk of infection after exposure is highly expected counseling of the HCW should be considered. Baseline HCV antibody test should be done for exposed HCW and retested at six weeks and six months, as well as checked for other blood borne pathogens. It is also recommended that HCV PCR testing be done at six weeks. Although the risk of transmission PCR negative HCW is negligible, but an antibody test at 6 months post exposure should be done to confirm that infection has not occurred.

In the case of exposed HCWs consulting with infectious disease specialist, expert clinical management of HCV is

recommended and HCV PCR and liver function tests should be undertaken during the window period. If HCV PCR found to be positive, the test should be repeated. If there is a doubt about acute seroconversion illness or HCV PCR positivity, urgent reference HCV PCR testing should be performed.

## Prevention

### *Pre-exposure prevention*

The key to reducing the incidence of HCV infection is decreasing exposure to contaminated blood. The incidence of post transfusion HCV infection has been reduced to very low levels by screening blood donations for HCV antibody as well as surrogate markers of HCV infection [5]. Although the impact is more difficult to measure, nosocomial HCV transmission in developing countries should decrease with worldwide adherence to universal precautions. There is some evidence that needle-exchange programs reduce HCV transmission among illicit drug users. However, most studies have not found reduced HCV transmission associated with needle exchange, and more work is necessary to prevent transmission in this setting [5].

### *Standard universal precautions*

The best way to prevent occupational transmission of all blood-borne pathogens is to prevent injuries and occupational exposure to blood [42]. For this purpose, health care providers should consider standard universal precautions [43,44]. Effective use of these precautions [45], reduce blood exposures and thus the risk of transmission of HCV. Elements of these precautions [45] include hand washing, use of protective barriers and attention to the appropriate use and disposal of needles and other sharp objects.

### *Post-exposure prevention*

Early studies provide conflicting data about the extent to which HCV Infection is modified by administration of pooled human immune globulin. However, because HCV seropositive donations are no longer included in the plasma pools from which immune globulin is manufactured, no benefit would be expected from products on the market today. Administration of immune globulin is not recommended following exposure to HCV in US Public Health Service guidelines.

An individual who has a documented exposure (e.g., a health care worker sustaining a needle stick from a patient who is known to be infected) should be screened for HCV antibodies as soon as possible after exposure to exclude prior infection. Serology and ALT testing should be repeated at least once, six months later. Most authorities also test HCV RNA two to four weeks after exposure, because interferon alfa is more effective when used early in the course of infection rather than years later [5].

### *Managing HCV infected HCW*

HCV transmission from HCW to patients has been reported infrequently, although several cases of iatrogenic transmission have been reported in the past few years [46,47]. The risk for HCW-to-patient HCV transmission during non invasive routine procedure is unlikely and during the performance of invasive procedures is very small [5]. In some countries restricting practices is implemented for HCV-infected HCW [48-50], but CDC has not recommended restricting the practices of HCW-HCV infected [48]. As is the case for all instances of managing HCW infected with blood-borne pathogens, each HCW should be evaluated individually. There is no definitive recommendation about anti

viral or immunomodulating therapy for HCW who are exposed to HCV.

### Conclusion

Information obtained from previous investigation on HCV infection has yielded a better knowledge about virology, natural history, immunology, magnitude of risk associated with occupational exposure to HCV in the health care workplace and treatment of hepatitis C infections. These data helps us to decide how to manage HCWs who are occupationally exposed to hepatitis C. Because data demonstrating the efficacy of any intervention are not yet available, no definitive post exposure anti viral therapy can be recommended for HCW care workers who are occupationally exposed to HCV.

Based on existing data from previous investigations, however, the preemptive therapy and watchful waiting strategies outlined in this review article represent reasonable interim approaches to this complex problem, until more definitive data become available in the future.

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