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REVIEW

Hidden hazards of HCV transmission

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Abstract Hepatitis C virus infection is a global health problem that has important epidemiological and clinical consequences. It has been well established that exposure to infected blood is the main risk factor for HCV transmission. However, in 20% of cases the agent transmission occurs by unknown route or in the presence of an unidentified source of infection. Understanding of the epidemiology of HCV is needed to help us define future control and preventive strategies. Herein, we discuss about diagnosis of HCV infection and hepatitis C surveillance in the context of its transmission.

Keywords Hepatitis C virus · Acute exacerbation · Chronic hepatitis · HCV transfusion-transmitted · HCV diagnosis · HCV infection

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Introduction

Hepatitis C virus (HCV) infection is a global health problem, and it is estimated that there are 170 million HCV carriers in the world [1]. The mechanisms that determine the clearance or persistence of HCV have not yet been elucidated. Both viral and host factors, such as HCV genotype and different vigor of the anti-viral cell-mediated immune response, can influence the disease's evolution [2]. Recently, it was demonstrated that variation in genes involved in the immune response—such as a single nucleotide polymorphism near the IL28B gene, which encodes the type III interferon—could enhance the resolution of HCV infection and contribute to the ability to clear the virus [3]. However, in the most infected individuals, this RNA virus evades the immune system and establishes a chronic infection that can lead to cirrhosis, liver cancer, and death [4].

It has been well established that exposure to infected blood is the main risk factor for HCV infection [5]. In the transfusion context, since the introduction of blood donor anti-HCV screening, the residual risk is essentially limited to the units collected during the donor's serological window period. However, this possibility has become so small that it cannot be accurately measured by traditional approaches, as prospective surveys of blood recipients, because of the limited number of documented transmission events [6]. Consequently, it can only be predicted by means of indirect measures, such as mathematical models involving the incidence of infection and the duration of the pre-seroconversion window period [7]. On the other hand, there are also risks associated with others modes of transmission linked to social, cultural and behavioral practices, involving percutaneous procedures, which has been related but poorly understood [8]. Despite these possibilities, in the most cases of HCV infection the source of infection or route of

transmission cannot be clarified. Besides, another problem about HCV transmission has been associated with the diagnosis of acute infection which can be difficult to prove. This occurs in due to, given the largely asymptomatic nature of the acute infection, the most patients with newly acquired HCV infection do not present with an acute hepatitis illness, and as a result few cases come to medical attention or are tested for evidence of HCV infection [9]. In this article, we discuss about surveillance and hepatitis C diagnosis in the context of its transmission.

Hepatitis C virus: transfusion and possible routes of transmission

With the serological test currently licensed, it is estimated that the residual risk of transfusion-transmitted HCV infection is 1 per 100.000 donations of according to the mathematic model of Schreiber et al. [7]. This occurs due to the limited capacity of HCV immunoserologic tests to detect blood infectivity only 70 days after acute infection (window period) [10]. Employment of genomic amplification tests (NAT) in donors screening allowed the detection of HCV infection about 50–60 days earlier than current antibody-based tests, resulting in a windows period of approximately 11 days, i.e., almost 80% of period reduction achieved by serological methods [10, 11]. Although implementation of these tests has significantly reduced the transfusion-transmitted HCV infection, it is known that there is a residual risk of acquiring hepatitis C through blood transfusions, which can range from 0.1 to 2.3 per million donations, depending on the region [6].

Although blood transfusion is the main way of HCV transmission, it is not the only one. It is recognized that hepatitis C virus infection can also occur through percutaneous injury using instruments with HCV-infected blood, such as, needles/syringes, piercing and tattoos instruments, nail clippers; major/minor surgery and dental procedures [12], besides the sexual transmission, although not being a classical and efficient route for HCV spread admitted, this possibility has not been rule out [13]. By the way, it is important to point out that 5% of all HCV cases occur by sexual route [14] and in 20% of cases, the agent transmission occur by unknown route, although RNA-HCV detection has been achieved from the saliva, breast milk, urine, feces, semen and cervico-vaginal secretions [14]. Additionally, it has been established that HCV perinatal transmission is possible, and the risk is approximately 5%, but breast-feeding has not been widely reported [15].

Although sexual transmission of HCV is inefficient and rarely admitted, outbreaks of sexually transmitted HCV infections have been reported among HIV-infected men who have sex with men (MSM), through linked molecular and clinical epidemiological studies [16–18]. Using phylogenetic analysis, HCV strains isolated from HCV-infected individuals have been compared with those isolated from MSM with HCV infection and revealed monophyletic clusters of MSM-specific HCV strains [17, 18]. From these findings, it has been possible to demonstrate increase of HCV infection prevalence among HIV-positive men and, also especially, support sexual HCV transmission [16, 18].

In mother to child transmission context, the exact time during pregnancy or delivery that HCV transmission occurs is unclear. It has been postulated that both "intrauterine" [19] and "intrapartum" [20] infections may occur, but the relative contribution by each route remains poorly quantified and difficult to establish. In a study to investigate when HCV infection from mother to child occurs and to evaluate possible associated factors, Mok et al. [21] tested 54 HCV-infected children within 3 days of birth and their mothers by HCV RNA PCR . It was showed that 17 of the children (31%) were positive in the first 3 days of life, and it could be assumed to have acquired infection in utero. In addition, 37 of the children (68%) were negative in the first 3 days of life but were positive when tested after 3 months. The results of this study suggest that at least one-third and up to a half of infected children acquired HCV infection in utero. However, similar studies are infrequent, and in the majority of cases the route of infection (whether intrapartum or intrauterine) remains unknown.

Although postpartum transmission is also recognized, the role of breast-feeding in transmission of hepatitis C virus has not been properly evaluated. It has been shown that among asymptomatic mothers, breast-feeding seems safe. On the other hand, symptomatic women, especially with high viral loads, should not breast-feed to avoid the risk of viral transmission through breast-feeding [22]. Thus, development of successful strategies to prevent mother to child transmission of HCV depends on understanding the timing of transmission, and associated factors, which has been difficult to assess [19].

Considering the possible routes of HCV transmission, several clinical procedures, such as, hemodialysis [23], endoscopy [7, 24, 25], invasive urologic procedures [26] and sclerotherapy [27], because inadequate cleaning of equipment or by the use vials multidose drugs and anesthetic, are risk factors and infection source, indicating possibility of nosocomial HCV transmission [28, 29]. This, indeed, may give from patient-to-patient, being this risk directly associated with the number and hospitalizations long time occurring in the same environment with infected individuals [27, 30]. In this context, the frequent percutaneous procedures provide many opportunities for contamination of surfaces and instruments with small amounts of HCV-infected blood, which frequent hospitalization associated and contact with the environment include risk factor to

HCV infection. Several reports indicate that medical treatment could be the cause of HCV transmission in some patients with acute hepatitis, and inadequate procedure was identified in most cases of suspected or proven nosocomial transmission of HCV [7, 27].

Obviously, it must be highlighted also the substantial risk of HCV transmission to health care workers in this environment, since it has been reported seroconversion of workers after percutaneous or mucocutaneous exposure to the blood or body fluids of HCV-infected patients [31, 32]. Similarly, it is of major importance to detect health care workers with HCV infection and establish regulations of how to deal with infected individuals working in specific health care setting, which currently there are not [33]. This strategy would also be of great value in prevention of health care worker-to-patient transmission of HCV.

However, cases of hepatitis C virus without infection source and transmission route could be clarified has been observed and described in literature. Recently, a 31-year-old woman was admitted at the hospital and underwent plastic abdominal surgery in January 2009 (case not published). On admission, the patient's serological status for HCV was not known. During surgery, she received two units of red blood. The HCV serological and molecular status of the blood donors was, respectively, determined by Murex Diagnostic HCV, version 4.0 and TMA HIV-1/HCV Procleix Assay Gen-Probe Incorporated (Chiron) with an estimated 100% detection limit for each single sample of 100 copies/ml. Two months after surgery, she demonstrated elevation of serum alanine aminotransferase (ALT) levels (870 U/l—Normal: <40 U/l) and was seropositive with OD of >3.000 and CO value of 0.705 in an anti-HCV immunoenzimatic assay (Murex Diagnostic HCV, version 4.0). By using NAT TMA HIV1/HCV Procleix Assay, the HCV infection was confirmed. Additional search for anti-HIV1 and anti-HIV2 antibody using the Genscreen kit (Biorad) was negative. Hepatitis B surface antigen (HBsAg) was negative as well as antibodies to HBsAg (anti-HBs) and antibodies to hepatitis B core antigen (anti-HBc), using Biorad assays.

The stored serum samples from each of two blood cells donors were tested again and confirmed negative using NAT TMA. The donors involved in that donation were notified, and in May 2009 another sample was collected for serological and molecular status HCV revaluation. They were negative for HCV infection. The patient had a history of blood transfusion in 2005, and there was no history of intravenous illicit drugs use. Her husband is negative for HCV.

Another case has been described in literature and highlights the difficulties to encounter and ascertain the actual cause of HCV infection among individuals who have neither injected drugs nor received blood or a blood product transfusion [8], or who has undergone another of risk events identified [34]. Accordingly, rigorous epidemiological studies on HCV infection have shown the prevalence of patients in whom it is not possible to identify any risk factor for acquiring the infection ranges from 10% [35] to 14% [36]. In addition, some studies have suggested the efficacy of the directed history is limited, and it has demonstrated that there is little benefit in routinely interviewing those HCV-infected people who have no history of injecting drugs or of having received a contaminated blood product transfusion [8]. This situation suggests that unknown routes of transmission, different from percutaneous route and from at-risk sexual contact, exist [37]. Among these routes, the sharing oral or nasal inhalation drugs equipments, as pipers or straws, could be included [38, 39].

Hepatitis C virus: acute infection or an acute exacerbation of chronic infection?

Hepatitis C virus infection can be divided into three clinical groups: "Resolved Infection" (15%), defined in patients who are anti-HCV antibody positive and HCV RNA negative and have normal alanine aminotransferase (ALT) levels; "Persistent infection/death" (15%), as in patients who are HCV antibody positive and HCV RNA positive and have elevated ALT levels; and, finally, "Benign persistence disease", involving approximately 70% of cases in which patients are HCV antibody positive and HCV RNA positive and have normal or mildly elevated ALT levels (CDC National Center for Infectious Disease Report, www.cdc.gov/ncidod/doseases/hepatitis/c,2001). However, what has been observed is that HCV acute infection diagnosis is difficult to be established. The investigation into IgM antibodies, the usual serological marker of acute infection, is unreliable in the context of HCV infection [40, 41]. Current algorithms for the diagnosis of HCV infection involve the detection of anti-HCV antibodies and/or HCV RNA in a serum sample. While such testing is able to distinguish between past, cleared HCV infection, and current infection, it does not allow discriminate between acute infection (or chronic) and an acute exacerbation of chronic infection [42]. In addition, the clinical diagnosis even in a patient presenting with an acute jaundice and possibly even a history of recent exposure may have an extremely low sensitivity—since the most of acute cases are asymptomatic (85–90%)—and will also have a low specificity, considering the impossibility to distinguish acute infection from an acute exacerbation of chronic infection [42].

In some countries of Europe, like England and Netherlands, there are surveillance systems to record new diagnosis of HCV infection based on the positive serology and

HCV RNA detection (HPAAR). Despite this strategy, these data are insufficient to distinguish between acute and chronic infection. In the USA, there is a similar scheme to report cases of acute viral infection implemented by CDC [43]. For HCV, the definition of acute infection case has both clinical and laboratory components. Despite including, it does not discriminate between acute infection and an acute exacerbation of chronic infection [42].

Cases of reactivation or recurrence of chronic hepatitis C, occurring after immunosuppressive therapy [44, 45], surgery [46], transplantation [47, 48] or even postpartum [49], have been described. Under the immunological point of view, these reports may be justified since on those clinical situations a immunosuppression established could be a factor predisposing to the viral agents reactivation such as, HBV, CMV (and other virus herpes), and HCV, as has been widely observed [50]. This finding, however, has only been possible when it is known the prior patient's serological status.

Even with the difficulties of establishing the HCV diagnosis infection acquired recently, some publications have shown that the illicit use of intravenous drugs is the largest risk factor for the acute cases [12, 13]. In accordance with Irving et al. [39], 54% of acute cases include intravenous drugs users' population, followed by 16% in individuals who underwent surgery, 10% associated with sex with known HCV-positive partner and 1.5% of cases by occupational exposure.

Conclusion

Although HCV is a transmissible disease, current management of HCV-infected patients in the most part of cases does not reflect this fact, due to epidemiologic and clinical disease aspects and natural history of infection. Thus, there are little standardized public health measures to deal with an infectious disease whose tracing contact and identification of the infection source is difficult, and the route transmission can be unknown. Considerable efforts have been implemented by governments and health departments in disease control. However, the impact of the applied strategies on prevalence and incidence of HCV infection has been hard to assess. Meanwhile, the find out of individuals with HCV infection in health care settings has long been recognized. HCV infection has been identified primarily by routine laboratory tests in the context of viral hepatitis surveillance or accidentally (as a result of screening protocols), a method that likely underestimates the magnitude of transmission. This means that the surveillance for hepatitis C typically is passive, with little or no capacity to investigate cases suggestive of transmission and to determine their true cause.

References

1. Kao JH, Chen DS (2000) Transmission of hepatitis C virus in Asia: past and present perspectives. J Gastroenterol Hepatol 15(Suppl): E91–E96
2. Hwang SJ, Lee SD, Lu RH (2001) Hepatitis C viral genotype influences the clinical outcome of patients with acute post-transfusion hepatitis C. J Med Virol 65:505–509
3. Thomas DL, Thio CL, Martin MP, Qi Y, Ge D, O'Huigin C, Kidd J, Kidd K, Khakoo SI, Alexander G, Goedert JJ, Kirk GD, Donfield SM, Rosen HR, Tobler LH, Busch MP, McHutchison JG, Goldstein DB, Carrington M (2009) Genetic variation in IL28B and spontaneous clearance of hepatitis C virus. Nature 461(7265):798–801
4. Tellinghuisen TL, Evans MJ, von Hahn T, You S, Rice CM (2007) Studying Hepatitis C virus: making the best of a bad virus. J Virol 81(17):8853–8867
5. Alter M (2006) Epidemiology of viral hepatitis and HIV co-infection. J Hepatol 44:6–9
6. Prati D (2006) Transmission of hepatitis C virus by blood transfusions and other medical procedures: a global review. J Hepatol 45:607–616
7. Schreiber G, Busch M, Kleinman S, Korelitz J (1996) The risk of transfusion-transmitted viral infections. N Eng J Med 26(334):1687–1690
8. Roy KM, Goldberg D, Taylor A, Mills P (2003) Investigation the source of hepatitis C virus infection among individuals whose route of infection is undefined: a study of ten cases. Scan J Infect Dis 35:326–328
9. Blackard JT, Shata MT, Shire NJ, Sherman KE (2008) Acute hepatitis C virus infection: a chronic problem. Hepatology 47(1):321–331
10. Giachetti C, Linnen J, Kolk D, Dockter J, Gillotte-Taylor K, Park M, Ho-Sing-Loy M, McCormick M, Mimms L, McDonough S (2002) Highly sensitive multiplex assay for detection of human immunodeficiency virus type 1 and hepatitis C virus RNA. J Clin Microbiol 7(40):2408–2419
11. Kolk D, Dockter J, Linnen J, Ho-Sing-Loy M, Gillotte-Taylor K, McDonough S, Mimms L, Giachetti C (2002) Significant closure of the Human Immunodeficiency Virus Type 1 and Hepatitis C Virus preseroconversion detection windows with a transcription-mediated-amplification driven assay. J Clin Microbiol 5(40):1761–1766
12. Idrees M, Riazuddin S (2008) Frequency distribution of hepatitis C virus genotypes in different geographical regions of Pakistan and their possible routes of transmission. BMC Inf Dis 8:69
13. Rè V, Gallego S, Farías A, Barbás G, Kremer L, Díaz M, Contigiani M (2008) Hepatitis C and HIV coinfection in central region of Argentina: prevalence, genotype characterization and risk factors. Enferm Infecc Microbiol Clin 26(7):423–425
14. Abou-Setta AM (2004) Transmission risk of hepatitis C virus via semen during assisted reproduction: how reals is it? Hum Reprod 12(19):2711–2717
15. Thompson S, Boughton C, Dore G (2003) Blood-borne viruses and their survival in the environment: is public concern about community needlestick exposures justified? Aust N Z J Public Health 27(6):602–607
16. Urbanus AT, van de Laar TJ, Stolte IG, Schinkel J, Heijman T, Coutinho RA, Prins M (2009) Hepatitis C virus infections among HIV-infected men who have sex with men: an expanding epidemic. AIDS 23(12):F1–F7
17. Danta M, Brown D, Bhagani S, Pybus OG, Sabin CA, Nelson M, Fischer M, Johnson AM, Dusheiko GM (2007) Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. AIDS 21(8):983–991

18. van de Laar TJ, van der Laar Bij AK, Prins M, Bruisten SM, Brinkman K, Ruys TA, van der Meer JT, de Vries HJ, Mulder JW, van Agtmael M, Jurriaans S, Wolthers KC, Coutinho RA (2007) Increase in HCV incidence among men who have sex with men in Amsterdam most likely caused by sexual transmission. J Infect Dis 196(2):230–238
19. Indolfi G, Rest M (2009) Perinatal transmission of hepatitis C virus infection. J Med Virol 81(5):836–843
20. Steininger C, Kundi M, Jatzko G, Kiss H, Lischka A, Holzmann H (2003) Increased risk of mother-to-infant transmission of hepatitis C virus by intrapartum infantile exposure to maternal blood. J Infect Dis 187(3):345–351
21. Mok J, Pembrey L, Tovo P-A, Newell M-L (2004) When does mother to child transmission of hepatitis C virus occur? Arch Dis Child Fetal Neonatal 90:156–160
22. Kumar RM, Shahul S (1998) Role of breast-feeding in transmission of hepatitis C virus to infants of HCV-infected mothers. J Hepatol 29(2):191–197
23. Otedo AE, McLigeyo SO, Okoth FA, Kayima JK (2003) Seroprevalence of hepatitis B and C in maintenance dialysis in a public hospital in a developing country. S Afr Med J 93(5):380–384
24. Sakai N, Tatsuta M, Iishi H, Yano H, Osaka S, Aoki A (2001) Effectiveness of manual cleaning and disinfection of gastroendoscopes with 3% glutaraldehyde for decreasing the risk of transmission of Hepatitis C virus. Am J Gastroenterol 96(6):1803–1806
25. Center for Disease Control and Prevention (CDC) (2008) Acute hepatitis C virus infections attributed to unsafe injection practices at an endoscopy clinic—Nevada. MMWR 57(19):513–517
26. Pekova L, Teocharov P, Sakarev A (2007) Clinical course and outcome of a nosocomial outbreak of hepatitis C in a urology ward. J Hosp Inf 67:86–91
27. Lédinghen V, Trimoulet P, Cazajous G, Bernard P-H, Schrive M-H, Foucher J, Faure M, Castéra L, Vergniol J, Amouretti M, Fleury H, Couzigou P (2003) Epidemiological and phylogenetic evidence for patient-to-patient hepatitis C virus transmission during sclerotherapy of varicose veins. J Med Virol 76:279–284
28. Froio N, Nicastri E, Comandini U, Cherubini C, Felicioni R, Solmone M, Di Giulio S, Petrosillo N (2003) Contamination by hepatitis B and C viruses in the dialysis setting. Am J Kidney Dis 42(3):546–550
29. Monsalve-Castillo F, Gomez-Gamboa L (2004) Hepatitis C virus. Iatrogenic and nosocomial transmition? Invest Clin 45(3):193–195
30. Forns X, Martinèz-Bauer E, Feliu A, García-Retortillo M, Martin M, Gay E, Nevasa M, Sanchez-Tapias J, Bruguera M, Rodes J (2005) Nosocomial transmission of HCV in the liver unit of a tertiary care center. Hepatology 41(1):115–122
31. Beltrami EM, Williams IT, Shapiro CN, Chamberland ME (2000) Risk and management of blood-borne infection in health care workers. Clin Microbiol Rev 13(3):385–407
32. Yazdanpanah Y, De Carli G, Migueres B, Lot F, Campins M, Colombo C, Thomas T, Deuffic-Burban S, Prevot MH, Domart M, Tarantola A, Abiteboul D, Deny P, Pol S, Desenclos JC, Puro V, Bouvet E (2005) Risk factors for hepatitis C virus transmission to health care workers after occupational exposure: European case-control study. Clin Infect Dis 41(1):1423–1430
33. Raggam RB, Rossmann AM, Salzer HJ, Stauber RE, Kessler HH (2009) Health care worker-to-patient transmission of hepatitis C virus in the health care setting: many questions and few answers. J Clin Virol 45(4):272–275
34. Wang CC, Krantz E, Klarquist J, Krows M, McBride L, Scott E, Shaw-Stiffel T, Weston S, Theide H, Wald A, Rosen H (2007) Acute hepatitis C in a contemporary US cohort: modes of acquisition and factors influencing viral clearance. J Inf Dis 196:1474–1482
35. Murphy E, Bryzman S, Glynn S, Ameti D, Thomson R, Willian A, Nass C, Ownby H, Screiber G, Kong F, Neal F, Nemo G (2000) Risk factors for hepatitis C virus infection in United States blood donors. Hepatology 31(3):756–762
36. Raguin G, Rosenthal E, Cacoub P, Veyssier P, Piette JC, Micoud M (1998) Hepatitis C in France: a national survey in the Departments of Internal Medicine and Infectious Diseases. The GERMIVIC (Joint Study Group on Hepatitis C Virus of the French National Society of Internal Medicine and the French Society of Infectious Diseases). Eur J Epidemiol 14(1):545–548
37. Ferrero MC, Dios PD, Scully C (2005) Transmission of hepatitis C virus by saliva? Oral Dis 11:230–235
38. Macías J, Palacios R, Claro E, Vargas J, Vergara S, Mira J, Merchante N, Corzo J, Pineda J (2008) High prevalence of hepatitis C virus infection among noninjecting drug users: association with sharing the inhalation implements of crack. Liver Inter 28(6):781–786
39. van den Berg C, van de Laar T, Kok A, Zuure F, Coutinho R, Prins M (2009) Never injected, but hepatitis C virus-infected: a study among self-declared never-injecting drug users from the Amsterdam Cohort Studies. J Viral Hepat 16:568–577
40. Coppola N, Pisapia R, Marrocco C, Martini S, Vatiero LM, Messina V, Tonziello G, Sagnelli C, Filippini P, Piccinino F, Sagnelli E (2007) Anti-HCV IgG avidity index in acute hepatitis C. J Clin Virol 40(2):110–115
41. Sagnelli E, Coppola N, Marrocco C, Coviello G, Battaglia M, Messina V, Rossi G, Sagnelli C, Scolastico C, Filippini P (2005) Diagnosis of hepatitis C virus related acute hepatitis by serial determination of IgM anti-HCV titres. J Hepatol 42(5):646–651
42. Irving W, Salmon D, Boucher C, Hoepelman I (2008) Acute hepatitis C virus infection. EuroSurveill 13(21):1–4 (pii: 18879)
43. Wasley A, Grytdal S, Gallagher K, Centres for Disease Control, Prevention (CDC) (2008) Surveillance for acute viral hepatitis—United States. MMWR Surveill Summ 57(2):1–24
44. Vento S, Cainelli F, Longhi M (2002) Reactivation of replication of hepatitis B and C viruses after immunosuppressive therapy: an unresolved issue. Lancet Oncol 3(6):333–340
45. Ennishi D, Yokoyama M, Terui Y, Takeuchi K, Ikeda K, Tanimoto M, Hatake K (2008) Does rituximab really induce hepatitis C virus reactivation? J Clin Oncol 26(28):4695–4696
46. Cardell K, Widell A, Frydén A, Akerling B, Mansson A, Franzén S, Lymer U, Isaksson B (2008) Nosocomial hepatitis C in thoracic surgery unit; retrospective findings generating a prospective study. J Hosp Infect 68:322–328
47. Molmenti E, Klintmalm G (2000) Hepatitis C recurrence after liver transplantation. Liver Transpl 6(4):413–414
48. Melon S, Galarraga M, Villar M, Laures A, Boga J, de Oña M, Gomez E (2005) Hepatitis C vírus reactivation in anti-hepatitic C virus-positive renal transplant recipients. Transpl Proc 37(5):2083–2085
49. Chen J, Chung J, Kao J, Chen D (2001) Post-partum acute exacerbation of chronic hepatitis in a hepatitis C-carrier mother. J Gastroenterol Hepatol 16(6):705–708
50. Humar A, Washburn K, Freeman R, Paya C, Mouas H, Alecock E, Razonable R (2007) An assessment of interactions between hepatitis C virus and Herpesvirus reactivation in liver transplant recipients using molecular surveillance. Liver Transpl 13:1422–1427