Hepatitis C Virus Infection and Kidney Disease

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ABSTRACT

Chronic hepatitis due to hepatitis C virus (HCV) infection is highly prevalent throughout the world. In addition to causing chronic hepatitis, HCV is associated with extrahepatic manifestations, especially renal. The exact mechanism through which HCV infection modulates the development and progression of kidney disease is unknown. Although several studies have examined an association of HCV infection with Glomerular Filtration Rate (GFR), their results have been inconsistent. On the other hand, studies have consistently found an association between HCV and albuminuria. Patients with unknown cause of proteinuria should be screened for HCV infection and upon positive results be closely followed up for signs and symptoms of deteriorating kidney condition.

Keywords: Hepatitis C virus infection; Chronic Kidney disease; Glomerular filtration rate; Proteinuria; Albuminuria

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INTRODUCTION

Chronic hepatitis due to hepatitis C virus (HCV) infection is highly prevalent throughout the world and is associated with heavy economic burden. Approximately 3.2 million individuals in the United States, 19 million in Europe, and between 130 and 170 million worldwide have HCV infection [1-3]. Chronic HCV infection is also associated with other liver diseases such as cirrhosis and hepatocellular carcinoma. In several countries, HCV-related liver disease is a major cause of liver transplantation [4]. Furthermore, HCV associated mortality had superseded HIV associated mortality by 2007 [5]. In addition to causing chronic hepatitis, HCV is associated with extrahepatic manifestations, such as renal, cardiovascular and metabolic [6]. Among various renal manifestations, HCV infection has been linked to membranoproliferative glomerulonephritis (MPGN) with type II mixed cryoglobulinemia, fibrillary glomerulonephritis, focal segmental glomerulosclerosis, interstitial nephritis, IgA nephropathy, and membranous nephpropathy [7]. Although several studies have examined an association between HCV infection and Chronic Kidney Disease (CKD), the results of these studies are inconsistent.

PATHOPHYSIOLOGY

HCV is an enveloped, spherical, single-stranded RNA virus from Flaviviridae family. HCV genome has single open reading frame flanked by 5' and 3' non-translated regions [8]. HCV is a blood-borne infection and, once infected, about 50-80% of patients develop chronic infection with HCV [1]. The process of HCV entry into the hepatocytes has three main steps. First, lipoprotein receptors and glycosaminoglycans capture HCV particles. Then, HCV particles interact with scavenger receptor class B type I, CD81, claudin-1, and occludin. Lastly, these interactions lead to cellular uptake of HCV [9]. Currently, seven HCV genotypes and 67 HCV subtypes have been identified [10].

The exact mechanism through which HCV infection modulates the development and progression of kidney disease is unknown. However, two mechanisms have been proposed. A direct cellular injury may be responsible for HCV-associated kidney disease as HCV virus RNA and proteins have been detected in the glomeruli and renal tubules [11-14]. On the other hand, deposition of circulating antigen-antibody complexes has also been proposed to cause renal injury although HCV antigen-antibody complexes have not been found in glomeruli [15]. However, mixed cryoglobulinemia (commonly associated with HCV infection) has been associated with various glomerular diseases [16, 17].

EFFECT OF HCV INFECTION ON GLOM-

-ERULAR FILTRATION RATE (GFR)

Although several studies have examined an association of HCV infection with GFR, their results have been inconsistent. In a large cross-sectional study (n=54,966) in an endemic area in Taiwan, Lee et al. found that HCV infection seropositivity was associated with 26% higher odds of low estimated GFR and was an independent risk factor for CKD [18]. In contrast, using the Third National Health and Nutrition Examination Survey (NHANES III), Tsui et al. found that HCV positive individuals had 5 ml/min (95% CI = 1, 9 ml/min, P=0.014) higher mean GFR than HCV negative individuals [19]. In a cohort study (n=167,569) with a mean follow-up of 25.3 months, Asrani et al. found that compared with HCV negative patients, fewer HCV positive patients had low GFR (45.6% versus 47.0%, P=0.02). Further, authors found no difference in progression to CKD in patients with and without HCV infection (3.8% versus 3.5%, P= 0.1) [20]. Similarly, in a retrospective cohort study including 474,369 adults from Medicare, Department of Veterans Affairs, and the United States Renal Data System, authors found that individuals with HCV infection were less likely to develop a decrease in GFR during follow up and the presence of HCV infection was associated with lower prevalence of CKD at baseline even after adjusting for confounding variables. However, when they developed a decline in GFR, the rate of decline tended to be faster in HCV infected individuals than in those not infected [21]. Li et al reached to the same conclusion in a population with CKD at baseline when they found increased progression of CKD in patients with HCV than those without [22]. Two additional cohort studies with CKD population at baseline found that HCV was associated with increased risk (greater than 2-fold and 2.14- fold, respectively) of developing end-stage renal disease [21, 23]. In contrast to above studies, Moe et al found no association of HCV infection with the prevalence, incidence, or progression of CKD (0.78, 95% CI = 0.66, 0.92) [24].

HCV AND ALBUMINURIA

As compared to the inconsistent results of studies examining the relationship of HCV with GFR, studies have consistently found an association between HCV and albuminuria. A meta-analysis of nine studies by Fabrizi et al. concluded that HCV was independently associated with protein-uria[25]. Results of three cross-sectional studies, of which two used NHANES III data and one was conducted in HCV/HBV endemic area of southern Taiwan, also found that HCV was significantly associated with proteinuria [19, 26, 27]. Similarly, Aoufi Rabih et al, found higher prevalence of microalbuminuria in HCV positive than in HCV negative patients [28]. Another recent study also found significantly higher levels of microalbuminuria in HCV positive than HCV negative patients (median 9.5 versus 5.9 g/mg, P=0.017) [29]. Glomerular injury to podocytes may be the underlying mechanism for HCV-associated proteinuria [30].

SUMMARY

Despite extensive research to determine relationship between HCV and CKD, the results are controversial. Contemporary studies show that HCV is associated with albuminuria and increase in GFR. The underlying physiological mechanism for these associations is unknown. One possible mechanism is that initial HCV-induced glomerular damage may trigger certain renal physiological responses to decreased permeability leading to changes in arteriolar resistance and thereby, increasing glomerular capillary pressure and favoring filtration. This mechanism could partially overcome effects of decreased permeability, at least initially, and then with the progression of the disease a rapid decline in GFR ensues. Thus, patients with unknown cause of proteinuria should be screened for HCV infection and upon seropositive results be closely followed up for signs and symptoms of deteriorating kidney condition.

REFERENCES

1. Pawlotsky JM. Pathophysiology of hepatitis C virus infection and related liver disease. *Trends Microbiol.* 2004; 12: 96-102.
2. Negro F. Epidemiology of hepatitis C in Europe. *Dig Liver Dis*. 2014; 46S5: S158-S64.
3. Hahne SJ, Veldhuijzen IK, Wiessing L, Lim TA, Salminen M, Laar M. Infection with hepatitis B and C virus in Europe: a systematic review of prevalence and cost-effectiveness of screening. *BMC Infect Dis*. 2013; 13: 181.
4. Boyer N, Marcellin P. Pathogenesis, diagnosis and management of hepatitis C. *J Hepatol*. 2000; 32: 98-112.
5. Ly KN, Xing J, Klevens RM, Jiles RB, Ward JW, Holmberg SD. The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. *Ann Intern Med*. 2012; 156 (4): 271-8.
6. Cacoub P, Gragnani L, Comarmond C, Zignego AL. Extrahepatic manifestations of chronic hepatitis C virus infection. *Dig Liver Dis*. 2014; 46S5: S165-S73.

7. Ozkok A, Yildiz A. Hepatitis C virus associated glomerulopathies. *World J Gastroenterol*. 2014; 20 (24): 7544-54.
8. Dubuisson J, Cosset FL. Virology and cell biology of the hepatitis C virus life cycle--an update. *J Hepatol*. 2014; 61: S3-S13.
9. Douam F, Lavillette D, Cosset FL. The mechanism of HCV entry into host cells. *Prog Mol Biol Transl Sci*. 2015; 129: 63-107.
10. Smith DB, Bukh J, Kuiken C, Muerhoff AS, Rice CM, Stapleton JT, *et al.* Expanded classification of hepatitis C virus into 7 genotypes and 67 subtypes: updated criteria and genotype assignment web resource. *Hepatology*. 2014; 59 (1): 318-27.
11. Sansonno D, Gesualdo L, Manno C, Schena FP, Dammacco F. Hepatitis C virus-related proteins in kidney tissue from hepatitis C virus-infected patients with cryoglobulinemic membranoproliferative glomerulonephritis. *Hepatology*. 1997; 25 (5): 1237-44.
12. Sansonno D, Lauletta G, Montrone M, Grandaliano G, Schena FP, Dammacco F. Hepatitis C virus RNA and core protein in kidney glomerular and tubular structures isolated with laser capture microdissection. *Clin Exp Immunol*. 2005; 140 (3): 498-506.
13. Okada K, Takishita Y, Shimomura H, Tsuji T, Miyamura T, Kuhara T, *et al.* Detection of hepatitis C virus core protein in the glomeruli of patients with membranous glomerulonephritis. *Clin Nephrol*. 1996; 45 (2): 71-6.
14. Cao Y, Zhang Y, Wang S, Zou W. Detection of the hepatitis C virus antigen in kidney tissue from infected patients with various glomerulonephritis. *Nephrol Dial Transplant*. 2009; 24 (9): 2745-51.
15. Roth D. Hepatitis C virus: the nephrologist's view. *Am J Kidney Dis*. 1995; 25 (1): 3-16.
16. Gragnani L, Fognani E, Piluso A, Zignego AL. Hepatitis C virus-related mixed cryoglobulinemia: is genetics to blame? *World J Gastroenterol*. 2013; 19 (47): 8910-5.
17. Tang SC, Lai KN. Hepatitis C virus-associated glomerulonephritis. *Contrib Nephrol*. 2013; 181: 194-206.
18. Lee JJ, Lin MY, Yang YH, Lu SN, Chen HC, Hwang SJ. Association of hepatitis C and B virus infection with CKD in an endemic area in Taiwan: a cross-sectional study. *Am J Kidney Dis*. 2010; 56(1): 23-31.
19. Tsui JI, Vittinghoff E, Shlipak MG, O'Hare AM. Relationship between hepatitis C and chronic kidney disease: results from the Third National Health and Nutrition Examination Survey. *J Am Soc Nephrol*. 2006; 17 (4): 1168-74.
20. Asrani SK, Buchanan P, Pinsky B, Rey LR, Schnitzler M, Kanwal F. Lack of association between hepatitis C infection and chronic kidney disease. *Clin Gastroenterol Hepatol*. 2010; 8(1): 79-84.
21. Tsui JI, Vittinghoff E, Shlipak MG, Bertenthal D, Inadomi J, Rodriguez RA, *et al.* Association of hepatitis C seropositivity with increased risk for developing end-stage renal disease. *Arch Intern Med*. 2007; 167 (12): 1271-6.
22. Li WC, Lee YY, Chen IC, Wang SH, Hsiao CT, Loke SS. Age and gender differences in the relationship between hepatitis C infection and all stages of Chronic kidney disease. *J Viral Hepat*. 2014; 21 (10): 706-15.
23. Su FH, Su CT, Chang SN, Chen PC, Sung FC, Lin CC, *et al.* Association of hepatitis C virus infection with risk of ESRD: a population-based study. *Am J Kidney Dis.* 2012; 60 (4): 553-60.
24. Moe SM, Pampalone AJ, Ofner S, Rosenman M, Teal E, Hui SL. Association of hepatitis C virus infection with prevalence and development of kidney disease. *Am J Kidney Dis*. 2008; 51 (6): 885-92.
25. Fabrizi F, Martin P, Dixit V, Messa P. Hepatitis C virus infection and kidney disease: a meta-analysis. *Clin J Am Soc Nephrol*. 2012; 7 (4): 549-57.
26. Liangpunsakul S, Chalasani N. Relationship between hepatitis C and microalbuminuria: results from the NHANES III. *Kidney Int*. 2005; 67 (1): 285-90.
27. Huang JF, Chuang WL, Dai CY, Ho CK, Hwang SJ, Chen SC, *et al.* Viral hepatitis and proteinuria in an area endemic for hepatitis B and C infections: another chain of link? *J Intern Med*. 2006; 260(3): 255-62.
28. Aoufi Rabih S, Garcia Agudo R, Tenias Burillo JM, Ruiz Carrillo F, Gonzalez Carro P, Perez Roldan F, *et al.* [Microalbuminuria and renal insufficiency in chronic hepatitis C virus infection]. *Gastroenterol Hepatol*. 2012; 35 (5): 309-16.
29. Derbala M, Shebl FM, Rashid A, Amer A, Bener A. Microalbuminuria in hepatitis C-genotype 4: effect of pegylated interferon and ribavirin. *World J Gastroenterol*. 2010; 16 (10): 1226-31.
30. Laurinavicius A, Hurwitz S, Rennke HG. Collapsing glomerulopathy in HIV and non-HIV patients: a clinicopathological and follow-up study. *Kidney Int*. 1999; 56 (6): 2203-13.