Executive summary of the 2018 KDIGO Hepatitis C in CKD Guideline: welcoming advances in evaluation and management

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Infection with the hepatitis C virus (HCV) has adverse liver, kidney, and cardiovascular consequences in patients with chronic kidney disease (CKD), including those on dialysis therapy and in those with a kidney transplant. Since the publication of the original Kidney Disease: Improving Global Outcomes (KDIGO) HCV Guideline in 2008, major advances in HCV management, particularly with the advent of direct-acting antiviral therapies, have now made the cure of HCV possible in CKD patients. In addition, diagnostic techniques have evolved to enable the noninvasive diagnosis of liver fibrosis. Therefore, the Work Group undertook a comprehensive review and update of the KDIGO HCV in CKD Guideline. This Executive Summary highlights key aspects of the guideline recommendations.

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The complete *KDIGO 2018 Clinical Practice Guideline for the Prevention, Diagnosis, Evaluation, and Treatment of Hepatitis C in Chronic Kidney Disease* is published simultaneously in *Kidney International Supplements*, volume 8, issue 3, 2018, which is available online at www.kisupplements.org.

Received 20 June 2018; accepted 29 June 2018

Kidney International (2018) **94,** 663–673; https://doi.org/10.1016/j.kint.2018.06.011

KEYWORDS: antivirals; chronic kidney disease; cryoglobulinemia; dialysis; direct-acting antivirals; glomerular diseases; guideline; hemodialysis; hepatitis C virus; infection control; KDIGO; kidney transplantation; liver testing; nosocomial transmission; screening; systematic review

The high prevalence of hepatitis C virus (HCV) in the chronic kidney disease (CKD) population has been recognized since diagnostic testing became available in the early 1990s, as was its transmission within dialysis units. Subsequent studies identified the adverse consequences of HCV infection in the CKD population, as well as its detrimental effect on recipient and graft outcomes following kidney transplantation. Although screening of blood products for HCV reduced its acquisition by blood transfusion, the unique aspects of the epidemiology of HCV infection in the CKD population were apparent. Studies established that transmission was frequent in dialysis patients and typically reflected insufficient attention to body fluid precautions. Also confounding the management of HCV in the CKD population was an absence of biochemical liver dysfunction in most

HCV-infected hemodialysis patients, which contributed to the lack of recognition of its presence and clinical significance. Furthermore, the toxicity of interferon (IFN) in this population underscored the need for effective and tolerable antiviral agents to treat HCV.

The initial Kidney Disease: Improving Global Outcomes (KDIGO) guideline, published in 2008, provided recommendations for the prevention, diagnosis, and management of HCV in CKD. Since then, there have been major advances in HCV management, particularly with the advent of direct-acting antiviral (DAA) therapy. In addition, diagnostic testing has evolved for the assessment of chronic liver disease. Therefore, we undertook a comprehensive review and update of the KDIGO HCV Guideline in patients with CKD.[1] All guideline recommendations are listed in Box 1, but it is beyond the scope of this Executive Summary to discuss each recommendation statement. Instead, we highlight significant concepts underlying the recommendations.

Chapter 1: Detection and evaluation of HCV in CKD

Initial screening. The majority of individuals with HCV infection are asymptomatic, making screening necessary to detect infection in high-risk populations; this is particularly true for hemodialysis patients in whom signs or symptoms of acute HCV infection are rarely recognized. Indeed, the prevalence of HCV infection is greater in CKD patients than in the general population, especially in those with advanced CKD who are not yet on dialysis therapy. In addition, HCV has been identified as an independent risk factor for both CKD onset and rapid CKD progression in multiple studies. Thus, HCV screening is recommended at the time of initial evaluation of CKD. HCV screening is also indicated for patients starting in-center maintenance hemodialysis and for those who transfer from another dialysis facility or modality. In dialysis units with a high prevalence of HCV, initial nucleic acid testing (NAT) should be considered. An HCV antibody (anti-HCV)−negative, NAT-positive profile strongly suggests acute HCV infection.

Screening of peritoneal dialysis and home hemodialysis patients should be considered upon initiation of dialysis to document baseline HCV infection status. If these patients transiently receive in-center hemodialysis, they should undergo HCV infection screening as per the recommendations for in-center hemodialysis patients. Kidney transplantation candidates should be tested for HCV infection during evaluation for transplantation for optimal management and planning.

Follow-up screening. Hemodialysis patients who are not infected with HCV should be screened for the presence of new HCV infection every 6 months using immunoassay. Acute HCV infection in a hemodialysis patient should be reported to the appropriate public health authorities, and all other patients in the same facility should promptly be evaluated by NAT to identify additional cases.

For anti-HCV-positive patients with chronic HCV infection who become HCV NAT-negative with a sustained virologic response (SVR) to DAA therapy, NAT screening should be initiated 6 months after documentation of SVR. SVR is assessed based on the results of NAT testing ≥12 weeks after the conclusion of therapy.

For patients with spontaneous resolution of acute HCV infection as documented by a negative test for HCV RNA at ≥6 months after the onset of acute infection, NAT screening should begin 6 months after documented resolution of infection.

Monthly monitoring of serum alanine aminotransferase is an inexpensive way to ensure that hemodialysis patients are assessed for possible acquisition of infection between regular antibody or NAT screenings. Even minor, unexplained alanine aminotransferase increases should raise the suspicion of acute HCV infection.

Evaluation of liver disease. All HCV-infected patients with kidney failure should undergo a noninvasive biochemical and/or morphological evaluation to stage liver fibrosis, determine the role and timing of antiviral therapies, and facilitate the choice of kidney or combined liver/kidney transplantation in cirrhotic patients. When biochemical and morphological evaluations yield discordant results or when liver comorbidities are suspected, liver biopsy is suggested.

Other testing. Although HCV infection predominantly causes liver disease, it is also associated with extrahepatic manifestations, including kidney disease. However, the relationship between HCV infection and CKD is complex. Based on current evidence, patients with HCV infection should be considered at increased risk of CKD, regardless of the presence of conventional risk factors for kidney disease. As such, all patients should be assessed for kidney disease at the time of HCV infection diagnosis with urinalysis and estimated glomerular filtration rate (eGFR) with repeat follow-up screenings if they are still viremic. Patients with HCV and CKD should be followed regularly to monitor progression of kidney disease.

An increasing body of evidence has implicated HCV infection in CKD progression.[1] Based on epidemiologic data, repeat testing for proteinuria and of eGFR in anti-HCV−positive/HCV NAT−positive patients is recommended. Overall, multiple studies have shown that HCV infection is associated with an increased risk of developing CKD, probably by multiple pathways, including accelerated atherosclerosis.

HCV is a blood-borne pathogen and shares routes of transmission with hepatitis B virus (HBV) and HIV. Although hepatitis A virus (HAV) infection is frequently benign in healthy individuals, superinfection with HAV and HBV in patients with liver disease (including chronic HCV infection) may result in significant morbidity and mortality. Thus, as HAV and HBV infections are preventable by vaccine, appropriate vaccination should be encouraged. However, it should be noted that response rates to vaccinations are diminished in patients with advanced CKD.

Chapter 2: Treatment of HCV infection in patients with CKD

Treatment recommendations are presented by CKD GFR category. For most CKD patients, as in the general population, the potential benefits of DAA treatment outweigh