

71538_Auto_Edited.docx

Name of Journal: *World Journal of Gastroenterology*

Manuscript NO: 71538

Manuscript Type: LETTER TO THE EDITOR

Comment on Review article: Chronic hepatitis C virus infection cascade of care in pediatric patients

Nouhoum Bouare *et al.* HCV CoC in Children

Nouhoum Bouare, Mamadou Keita, Jean Delwaide

Abstract

An enhanced cascade of care (CoC) should include a younger population, helping to achieve the goal of the World Health Organization (WHO) with a focus on elimination in the pediatric population. Furthermore, enhanced screening and awareness efforts and continued education of health care providers will improve the outcomes of chronic hepatitis C virus (HCV) infection in the pediatric population. The present work discusses and comments on the topic (cascade of care in HCV chronic pediatric patients) addressed and reported by Rogers ME and coworkers.

Key Words: Cascade of care; HCV; Chronic patients; Pediatric population; Disease management; Commentary

Bouare N, Keita M, Delwaide J. Comment on Review article: Chronic hepatitis C virus infection cascade of care in pediatric patients. *World J Gastroenterol* 2021; In press

Core Tip: Wide worldwide disparities exist regarding the chronic hepatitis C virus infection cascade of care (HCV CoC), and it is most evident between high-income countries and areas with scarce resources. An integrative strategy encompassing efficient pediatric HCV diagnosis and treatment as well as prevention is needed. Addressing health care disparities by insightfully applying successful outcomes from high-income countries in certain disadvantaged regions with poor CoCs may help to achieve the elimination goal set by achieve the WHO HCV.

TO THE EDITOR

COMMENTARY

To eliminate viral hepatitis worldwide by 2030, the WHO focused on strategic objectives to reach a decrease of 90% and 65% the disease incidence and mortality respectively ^[1, 2]. The cascade of care (CoC) originates from HIV management aimed in some an extent to achieve sustained virological response (SVR) ^[2]. It addresses the

diagnosis, treatment, and possible cure of HCV [1,2]. HCV chronic infection is reported as affecting 71 million of persons globally, and many of them unaware their infectious status [3]. The global HCV and HBV populations remain largely underdiagnosed and undertreated [4]. For worldwide heterogeneity, reliable HCV prevalence estimates (adjusted to age and geographic area) are needed. These country-specific estimates can highly improve the intervention by accelerating HCV elimination [1].

Rogers *et al.* [1] reported a number of field epidemiological and/or clinical factors impacting disease evolution. Perinatal route is mainly pointed as responsible of the HCV infection propagation in pediatric population. This route is reported as favorable to genotype 1a that is even associated with decreased clearance, persistent viremia and the risk of liver damages such as end-stage liver disease in treatment-naïve children. High grade fibrosis or cirrhosis patients are still at high risk to develop hepatocellular carcinoma (HCC) even if achieving SVR. Histological studies are still needed to support direct acting antiviral (DAA) treatment efficacy. The authors noticed the need of fibrosis control in children regarding the constant risk of portal hypertension and hepatocellular carcinoma occurrence. Moreover, poor social act and health-related quality of life were described in adolescents HCV patients [1]. Delaying treatment until 18 year of age favors lifetime risk of avoidable late liver complications. Hence early treatment is economic and lifesaving [1].

However, HCV CoC reports, similar to that of Rogers and coworkers, mostly emanate from high-income countries [2]. Extending an HCV CoC strategy to low- and middle-income areas must initially and insightfully focus on disease awareness and education to disseminate the desired global health goal. Moreover, addressing the differences between a CoC applicable in high-income countries and another adjusted for low-income areas is central to achieving the ultimate HCV elimination goal.

Regarding HCV therapy, DAAs highly impact CoCs. However, in 2016, the treatment was less accessible for the patients. As for CoC, updated estimates is needed to assess the impact of new implemented approaches aimed to promote hepatitis C eliminating [5]. Furthermore, improving the linkage to care is lifesaving given the precipitous

dropouts occurring in HCV CoC [6]. Rogers *et al.* [1] reported innovative intervention approaches to promote HCV management through an academic mentorship program. This program intended to build a model that could improve the health of underserved communities in Appalachian region. It has even reinforced the competences of primary health care providers to treat patients on site, thus reducing the need for travel to seek a DAA therapy specialist. The advent of telemedicine has also had a positive impact on HCV treatment. Extension for community health care outcomes (ECHO) through videoconferencing technology may be useful for HCV treatment in underserved communities [1].

This educative, extensive and informative model, combined with efficient and reliable HCV diagnostic and treatment efforts among pediatric patients along with preventive tools, should thoroughly address the hepatitis C elimination goal worldwide. The simultaneous screening of three viral infections (HIV, HCV and HBV) using a multiplex immunochromatographic rapid diagnosis test (HCV/HBsAg/HIV Combo RDT Cassette [ITHD-C43], Biotest Biotech Inc, Hangzhou, China) in childbearing aged women may reinforce the prevention against these diseases [7]. This multiplex test may be useful in sub-Saharan Africa because it improve in full the “cascade of screening” at once, and linkage to care with reduced cost [7].

The electronic medical record (EMR)-based screening programs are also recommendable for low-income areas since determined to be an effective method to manage patients for HIV and HCV in Appalachian region [8]. Among the primary preventive means, we can enumerate campaigns for behavioral changes in high-risk groups, such as persons who inject drugs (PWID), and surveillance of pregnant women and diabetic and nonhepatic cancer patients.

However, high treatment costs and small numbers of trained providers are the primary reasons for slow HCV comprehensive elimination in low-income areas [9]. Successful efforts toward HCV elimination among PWID contrast with the relative lack of attention to scarce resource settings where the hopes and potential for elimination are less clear, such as in many low- and middle-income countries (LMICs) [10]. In addition,

pretherapeutic tests and treatment access are still challenging in developing countries [11]. CoC is a major challenge in regard to prison setting. Post release interventions that integrate HCV care are highly effective. The treatment observance can be highly improved by a close collaboration between community and prison health care programs. Investigations are still needed to determine predictors of linkage to HCV care after release [12].

To overcome these barriers mentioned above, an efficient model for HCV CoC should be simple, targeted, pluralistic, scalable, integrated, patient-centered and affordable [13].
1 Efforts should focus on linkage to care to capitalize on DAA treatment advances and increase patients access to Medicaid assurance [14]. Regular follow-up of patients greatly increase HCV therapy effectiveness. Modelling studies show that a perfect follow-up would be cost-effective. Multilevel interventions along the cascade should be prioritized rather than single level [15]. Interventions that promote chronic hepatitis B/C elimination can be summarized as follow: prioritize management of patients at multiple levels of the health care setting; define the required supports enabling to notice unassessed patients; expand disease management skill in a variety of settings; promote harm reduction services [16].

Moreover, if major price reduction achieved by HIV/AIDS community can be applied to HCV, a similar success story could emerge [17]. Domestic program and funding are ongoing implemented in many middle-income area to support large scale DAA treatment, intended to achieve the WHO HCV elimination objective. However, investments required to achieve the WHO related elimination targets are insufficient given the feeble contribution from domestic financing sources and weakness of international funding for HCV programs. In fact, Unitaid partnership is starting with some countries to simplify and decentralize HCV CoCs for a large scale feasibility. This donor is even encouraging coordination among other partners working in the field to support the Global Hepatitis Program for better response [18]. Models of service delivery are being piloted and implemented throughout the Western Pacific Region, which will support “learning by doing”, in the delivery of hepatitis testing, care and treatment

tailored to countries' unique health contexts ^[19]. Malaysia launched universal coverage of free testing and treatment for HCV in March 2018, with rapid expansion of services to decentralize testing and treatment in primary care clinics in 2019. In Vietnam, pilot programs are in progress to assess the feasibility of decentralizing HCV testing using point-of-care diagnostics to screen in different settings. In China, the entry of DAAs into the market changed conversations on the possibility of eliminating HCV and improving large-scale access to treatment. Many high-income countries in the Asian region universally covered hepatitis testing, care and treatment through government financing and health insurance. However, challenges remain regarding vulnerable populations, including PWID, incarcerated populations, migrants and indigenous people. These challenges involve increasing testing access and connection to care after diagnosis, improving public awareness of hepatitis B and C, training health care providers, particularly at the primary care level, and addressing stigma and discrimination. Medicines (DAAs) have revolutionized treatment for HCV, and they are becoming available in many LMICs, even if the cost can barely be borne by patients in a large majority of these countries. The market for generics has developed quickly but is volatile due to fluctuations in demand combined with inconsistent and insufficient financing. In the Asian region, affordability has improved as generic medicines have become more widely available. In countries where medicine prices remain high, access is limited by rationing and cost containment. On the other hand, where cheaper generics are available, financing and affordability by those most affected by HCV can still be a major barrier to access. Out-of-pocket expenses vary widely across the Asian region and are still a significant barrier to access. There are significant differences in how countries control the prices of medicines, ranging from free pricing to single-payer, controlled pricing arrangements. Countries with single-payer systems achieved significant price controls for the new DAAs by using their monopoly purchasing power. For example, the Australian Department of Health negotiated a five-year volume-based price deal based on treating 62,000 people for AU\$ 1 billion. Over 38,000 people were treated in the first year. This innovative approach removed price as a barrier to

treatment. In New Zealand, the advantage of the Pharmaceutical Management Agency (PHARMAC) helps to secure favorable prices for medicines in negotiations with suppliers. Similar purchasing strategies could be used in other countries where medicines are financed by the government. Greater sharing of information on prices and negotiation strategies across the region is important to improve access to expensive medicines. Another option for accessing affordable hepatitis medicine has been to take advantage of commercial agreement related Intellectual Property Rights *a fortiori* in LMICs [19]. As far as HCV CoC is concerned, interesting and successful decentralized public health programs and government support have been experimented in Africa (Rwanda, for instance) and Asia [20]. Moreover, Rwanda and Egypt have incredibly developed their national HCV programs in line with the WHO elimination targets, as reported by Rajiv S *et al.* [21]. However, to reach the above targets, sub-Saharan African region must still overcome several barriers. Important investments and political engagement are needed to overcome these challenges [21]. From the period 2014 up to 2020, Egypt undertaken a vast campaign of HCV screening and treatment in line with disease elimination purpose. In fact, more than 50 million of residents were screened for chronic HCV (whose 4 million treated). The key successful elements noticeable were as follow: reliable epidemiological surveillance; robust public health system; inclusive care open to all social sectors; increased health care spending; and innovative research and use of new technologies of communication. Egypt is suggested to be the first country in order to eliminate HCV out of its territory. This expertise can be useful for other LMICs with high HCV burden [22].

As far as the WHO HCV elimination goal is concerned, Mali has included viral hepatitis in the category of priority diseases through the promulgation of Law No. 2019-021 of July 3, 2019, which creates the sectorial unit to fight HIV/AIDS, tuberculosis and viral hepatitis (CSLS-TBH) and takes these diseases into account in the ten-year social health development plan (PDSS) 2014-2023. In this country, despite the political will that has been shown, there are still difficulties such as low level of knowledge of health workers on viral hepatitis; insufficient human resources, infrastructure and reagents for the

management of viral hepatitis; financial and geographic (for the patients who reside outside Bamako) inaccessibility to antivirals [23]. The care centers for HCV patients, mainly made up of hepato-gastroenterology, infectious diseases and internal medicine departments, are concentrated in Bamako (the capital of Mali). DAA medicines such as sofosbuvir in combined with ledipasvir or velpatasvir, which are not provided in management centers, are sold at a high price in private pharmacies. These drugs are not covered by governmental compulsory health insurance. Other factors limiting access to treatment are the high costs of pretreatment investigations (170,000 XOF by patient for HCV) [23].

The next key steps to strengthen interventions include sustained efforts to reach major cost reduction of HCV management (for instance promotion of both generic DAAs and diagnosis tests) in all countries at a level comparable to HIV pricing; recording potential generic drug manufacturers at country level; improvement of domestic and donor funding; reinforcing of monitoring and evaluation system, by using digital tools to tract patients and manage stock; integration with programs such as : HIV and sexually transmitted diseases, harm reducing service, primary health care and reproductive health; decentralization and task delegation service; and further community engagement. Furthermore, early management of disease is important because it is cheaper to treat HCV early than treat complications *a fortiori* in LMICs where resources are scarce [20].

CONCLUSION

Pediatric patients with liver fibrosis evidence must be regularly monitored given the constant risk of portal hypertension and hepatocellular carcinoma occurrence. Early treatment can save money and lives. Furthermore, the actions taken to improve access to health care in certain disadvantaged regions of high-income countries, as seen in the Appalachian region, can be usefully employed in low-income countries.

ORIGINALITY REPORT

1%

SIMILARITY INDEX

PRIMARY SOURCES

1	www.ncbi.nlm.nih.gov Internet	16 words — 1%
---	--	---------------

EXCLUDE QUOTES ON
EXCLUDE BIBLIOGRAPHY ON

EXCLUDE MATCHES < 12 WORDS