

Hepatitis C in Sub-Saharan Africa: Urgent Need for Attention

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The hepatitis C virus (HCV), which was not recognized as an infectious agent until the 1980s, is responsible for a worldwide epidemic. The World Health Organization estimates global prevalence at 2.8%, with 185 million persons infected. In contrast to hepatitis B, where successful vaccine campaigns have reduced the disease burden, much less progress has been made toward the control of HCV. Phylogenetic studies suggest that HCV originated in Africa and has been endemic in some regions for at least 500–600 years. However, little is known about the epidemiology, transmission, and clinical course of HCV in Africa. With the advent of highly effective anti-HCV agents, there exists great potential to at least curb the global epidemic. For regions such as sub-Saharan Africa, however, this will require a thorough understanding of the regional population-level epidemiology, risk factors, and transmission mechanisms. Only then can effective treatment and prevention strategies be introduced.

Keywords. Africa; epidemiology; hepatitis C; transmission.

More than 185 million individuals have been infected with hepatitis C virus (HCV), and 80% of them have chronic HCV infection, 5 times more than with human immunodeficiency virus (HIV) [1]. The global epidemic of HCV is disparate, with high levels of disease burden in low-income regions; sub-Saharan Africa (SSA) accounts for nearly 20% of global infections. New, highly effective agents provide promise for cure in treated individuals, and advent of these new agents has appropriately refocused attention on this public health threat. However, attention to cure this virus with drugs should not divert efforts away from SSA, where traditional prevention by disrupting transmission is still critical.

SUB-SAHARAN AFRICA: TRUE DISEASE BURDEN OF HCV?

Although it was first recognized in the 1980s, HCV is now the cause of a global epidemic, and in some regions it is the leading cause of cirrhosis, liver failure, and cancer. The World Health Organization (WHO) estimates that more than 185 million persons are infected with HCV, substantially higher than HIV rates. Sub-Saharan Africa has some of the highest reported global rates of HCV seroprevalence, ranging from 2.1% to 2.8%, with the highest in West Africa, approximately 2.8% (95% confidence interval, 2.4–3.3). Although age-specific prevalence rates peak at 55–64 years of age, with estimates from 5% to 3.67%, a 2-peak pattern has been observed in West Africa, with a lower but distinct peak apparent in the 15- to 19-year-old age group [1]. These estimates are conservative, because the comprehensive meta-analysis compiling these estimates excluded high-risk populations. Representative surveys were not available from SSA, and evidentiary support for these estimates is listed as moderate, with limited number of data point entries.

The wide variability in testing modalities is further complicating our understanding of basic prevalence

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estimates across SSA. Several studies have suggested high false-positive rates to HCV serologic assays. For example, Seremba et al [2] found substantial variation between rapid screen assays (RSAs) and enzyme immunoassays and detected active viremia in only 29.1% of those positive on serologic assays (14 of 48). In a study in Uganda, no viremia was detected in the 7.6% of 1000 individuals who were HCV antibody positive [3]. Other studies found conflicting results, which highlights the distinct possibility of localized outbreaks. In 2 rural villages in Nigeria studied by the Centers for Disease Control and Prevention, seroprevalence was 15% using an RSA [4]. Of those positive, 82% had detectable viremia, suggesting both a high rate of exposure and active infection. In our own study based in Ghana, 74%–88% of individuals confirmed as seropositive had detectable virus, depending on the serologic assay used to define seropositivity (unpublished data).

Both the wide variation in assays used and sample storage parameters that impact RNA stability are distinct but important reasons for such varied results. Different generation assays, including rapid screen assays, have been used in past studies that vary in sensitivity and specificity. The relevance of specimen handling and storage procedures is even more important. Few past reports have provided details about specimen handling and processing. Ribonucleic acid is susceptible to degradation, especially with temperature fluctuations. Maintaining proper temperature control and shipping specimens while maintaining sample integrity are complicated but critical components of conducting research in SSA. These problems may have affected some reported prevalence studies. It is paramount that for future studies on HCV in SSA, careful attention should be paid to testing strategies and sample handling and storage, and these details should be included in research reports.

HEPATITIS C VIRUS IN AFRICA: UNRESOLVED HEPATITIS C VIRUS EPIDEMIOLOGIC QUESTIONS

The limitations of our knowledge extend beyond the uncertainty of seroprevalence to nearly all aspects of the HCV epidemic in SSA. The rarity of community- or population-based studies prevents us from understanding risk factors for acquisition and disease progression, a fundamental first step toward screening and prevention. Although the main modes of transmission in Western countries are well understood, the exposure risks in Africa are less clearly defined. Unsterile needles and transfusion of blood products have no doubt played a role, but the varied genotypes and high diversity seen in circulating strains, and lack of similar cohort exposures in SSA populations, compared with that seen in Egypt, do not suggest that transmission of HCV has occurred from a singular mode across SSA. Furthermore, it remains unclear what routes would have allowed the virus to be endemic for several centuries, as suggested by the high level of diversity seen in circulating strains. No doubt, some proportion of the

Table 1. Uncertainties of HCV in Sub-Saharan Africa

Unknown Aspects of HCV in Sub-Saharan Africa	Potential Research Strategies
Appropriate serologic/diagnostic testing	<ul style="list-style-type: none"> - Validation/comparison studies - Attention to specimen storage/shipment that may alter serologic and virologic assays - nucleic acid testing to confirm seroprevalence data
True population level epidemiology	<ul style="list-style-type: none"> - Population level cohorts, accounting for age, migration, and varied geographic regions
Risk factors/transmission mechanisms	<ul style="list-style-type: none"> - Epidemiologic risk factor analyses - Molecular/phylogenetic network analyses - Social network/cluster analyses
Level of chronicity	<ul style="list-style-type: none"> - Chronic infection cohorts
Relevance of known viral diversity	<ul style="list-style-type: none"> - Molecular/virologic/genetic studies
Treatment effectiveness	<ul style="list-style-type: none"> - Treatment studies/clinical trials

Abbreviation: HCV, hepatitis C virus.

sharp increase in HCV during the 20th century in Africa must be attributable to the introduction of parenteral therapies and blood products; however, with advances in blood screening and better knowledge of the danger of shared needles in the medical community, these exposures likely account for a decreasing percentage of recent incident cases. The bimodal age group peaks seen in data from West Africa further implies that the transmission modes and risk factors may vary across age groups and age cohorts. Studies have found associations with cultural or traditional practices, such as scarification, tribal markings, home circumcision and birth, as well as the possibility of intrafamilial transmission. However, the relative significance of these modes needs to be elucidated. Other knowledge gaps span the spectrum from incomplete data on genotypes circulating in SSA to minimal knowledge on chronicity and character of disease progression (Table 1). Liver cancer is one of the most common cancers in SSA, especially in men. Although hepatitis B virus and aflatoxin are major contributors to hepatocellular carcinoma (HCC) in SSA, chronic HCV infection is no doubt an important causal factor in this deadly cancer. Studies may be limited in their ability to estimate the impact of chronic HCV infection in the etiology of HCC in SSA because of limited reliable population-based data on HCV prevalence. Increased knowledge of all these aspects of HCV disease is prudent for targeted primary and secondary prevention efforts.

HEPATITIS C VIRUS IN SUB-SAHARAN AFRICA: KNOWLEDGE GAINED EXTENDS BEYOND THE CONTINENT

Although the utmost priority is to curb the epidemic of HCV in SSA, it is important to recognize that the knowledge gained

from studying HCV in SSA potentially has broad significance for the field. With our mobile world population, understanding the epidemic has implications for the care of travelers and immigrants from these regions. Well described racial disparities are observed in the epidemiology of HCV in the United States, and allelic variation in the IFNL3/4 explains some but not all of these findings. Therefore, study of African cohorts provides the opportunity to shed light on the host and viral factors that could in part account for the noted racial disparities between black and non-black Americans.

ADDRESSING HEPATITIS C VIRUS IN SUB-SAHARAN AFRICA: THE TIME IS RIGHT

Highly effective new HCV antiviral medications are now available, and more drugs will reach the market soon. The WHO has produced updated guidelines recommending the treatment of individuals with chronic HCV infection [5]. However, critical issues must be surmounted to bring such important recommendations to fruition. Current costs prohibit treatment in most low-income countries. Treatment decisions require sophisticated laboratory capacity, because the appropriate treatment regimen and duration depend on assessment of viral genotype and potential viral mutations. Treatment also requires frequent access and visits to healthcare systems. Newer agents should obviate some of these requirements. Training of healthcare providers would be essential in regions not versed or with inadequate capacity to administer treatment. Such issues will need to be overcome to initiate effective treatment campaigns.

Treatment campaigns require effective screening and referral to care. The most recent WHO guidelines highlight varied screening approaches, recommending targeted screening of individuals with high-risk behaviors, or those who reside in high

prevalence areas [5]. For much of SSA, the latter would apply, but it is not possible to test the entire population. Implementation of targeted screening by risk factors would require an understanding of the population-level epidemiology in SSA countries. Scientifically sound data on such parameters is sorely missing. Without an HCV vaccine available, treatment may also play an important role in prevention measures. However, caution must be noted, because successful treatment does not prevent reinfection. Primary prevention efforts must also play a paramount role for both reduction of new infections as well as reinfection.

We believe it is critically important to better understand the epidemiology of HCV in SSA now. This approach will require a multilevel, short- and long-term strategy. Efforts to address cost and infrastructural capacities necessary for eventual treatment should begin, but it will take time. In the interim, immediate attention to define the population level epidemiology, current risk factors, and transmission mechanisms of HCV in SSA need to be addressed (Table 1). Such studies will pave the pathway for successful treatment and prevention efforts.

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