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Epidemiology of viral hepatitis and HIV co-infection

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Worldwide, hepatitis B virus (HBV) accounts for an estimated 370 million chronic infections, hepatitis C virus (HCV) for an estimated 130 million, and HIV for an estimated 40 million. In HIV-infected persons, an estimated 2–4 million have chronic HBV co-infection and 4–5 million have HCV co-infection. HBV, HCV and HIV share common routes of transmission, but they differ in their prevalence by geographic region and the efficiency by which certain types of exposures transmit them. Among HIV-positive persons studied from Western Europe and the USA, chronic HBV infection has been found in 6–14% overall, including 4–6% of heterosexuals, 9–17% of men who have sex with men (MSM), and 7–10% of injection drug users. HCV infection has been found in 25–30% of HIV-positive persons overall; 72–95% of injection drug users, 1–12% of MSM and 9–27% of heterosexuals. The characteristics of HIV infected persons differ according to the co-infecting hepatitis virus, their epidemiologic patterns may change over time, and surveillance systems are needed to monitor their infection patterns in order to ensure that prevention measures are targeted appropriately.

***Keywords*: Hepatitis C; hepatitis B; HIV; Prevalence; Co-infection**

1. Introduction

Hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) are among the top 10 leading causes of infectious disease deaths worldwide (1). Globally, chronic infection with each of these viruses alone contributes to substantial morbidity; HBV infection accounts for an estimated 370 million chronic infections, HCV infection for an estimated 130 million, and HIV infection for an estimated 40 million (2–4). These viruses share common routes of transmission, but they differ in efficiency by which certain types of exposures transmit them and in their prevalence by geographic region.

2. HBV infection

The endemicity of HBV infection is influenced primarily by the age at which most infections occur (5). Endemicity of infection is high in those parts of the world where almost all infections occur during the perinatal period or early in childhood (for example, Southeast Asia and sub-Saharan Africa). At least 8% of the population in these areas is chronically infected and 70–90% has serological evidence of previous HBV infection. Risk of HBV infection continues after the first 5 years of life, but its eventual contribution to the high rate of chronic infection is less significant. In areas of the world with an intermediate endemicity of HBV infection (for example, Eastern Europe, Middle East, and Russia), there are mixed patterns of infant, early childhood and adult transmission. The prevalence of chronic infection ranges from 1 to 7% of the population and serological evidence of past infection is found in 10–60%. In most developed parts of the world (for example, Western Europe, Australia, USA), the endemicity of HBV infection is low and most infections occur among high risk adult populations that include injection drug users, persons with multiple heterosexual partners, and men who have sex with men (MSM). The prevalence of chronic HBV infection is $<1\%$ and the overall infection rate is 5–7%.

HBV is transmitted by percutaneous and mucous membrane exposures to infectious blood and body fluids that contain blood (5). Percutaneous exposures that have resulted in HBV transmission include transfusion of blood

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or blood products, contaminated equipment used for therapeutic injections and other health-care related procedures, illegal injection drug use, and needle sticks or other injuries from sharp instruments sustained by hospital personnel. In addition, occasional outbreaks of hepatitis B have been associated with tattooing and acupuncture. Perinatal and sexual exposures to HBV are also highly efficient modes of transmission, and person-to-person spread of HBV can occur among household contacts of a chronically infected person, likely as a result of non-intact skin or mucous membrane contact with secretions containing blood.

In most developed countries, the highest incidence of acute hepatitis B is among young adults (6–11). In Western and Southern Europe, high-risk sexual activity (heterosexual and MSM) accounts for most cases of newly acquired hepatitis B (6–8); in Northern Europe and the UK, injecting drug use accounts for most cases (9,10). However, even in these low HBV endemic countries, a substantial number of children become infected with HBV, many of whom belong to families that have emigrated from high HBV endemic countries; they can account for a disproportionately high number of chronic HBV infections (12,13).

Transmission of HBV via transfusion or transplant has been virtually eliminated in countries that test donors for HBsAg and virally inactivate plasma-derived products (14). However, other healthcare-related procedures have continued to result in episodes of HBV transmission from one patient to another (15–20). In most cases, these transmissions resulted from non-compliance with aseptic techniques and recommended infection control practices that were designed to prevent post-procedure infections due to cross-contamination of medical equipment and devices. In developing countries, donor testing for HBsAg is not universal and transmission through unsafe therapeutic injection practices, including inadequately sterilized needles and medical instruments, the reuse of disposable needles and syringes, and contamination of multiple dose medication vials remains a significant problem (21).

3. HCV infection

The estimated worldwide prevalence of HCV infection is 2.2% (3). Similar to HBV, geographic differences in the endemicity of HCV infection can be described based on regional prevalences; high (prevalence $\geq$3%) moderate (prevalence 2–2.9%), low (prevalence 1.0–1.9%), and very low (prevalence $<$1.0%) (3,22). However, the regions corresponding to these prevalences are different for HCV than for HBV. Highest prevalence of HCV infection has been reported from Northern Africa (particularly Egypt), moderate prevalence from Eastern Europe and most of Asia, low prevalence from Western Europe, North and South America, and Australia, and very low prevalence from Northern Europe and the UK.

Risk factors associated with acquiring HCV infection include transfusion of blood and blood products and transplantation of solid organs from infected donors, illegal injection drug use, unsafe therapeutic injections, occupational exposure to blood (primarily contaminated needle sticks), birth to an infected mother, sex with an infected partner, and sex with multiple partners (23). Among these, transfusion from unscreened donors, injection drug use, and unsafe therapeutic injections have been the most important; however, there are temporal and geographic differences in the extent to which these risk factors have contributed to HCV transmission.

In high prevalence and many moderate prevalence countries unsafe therapeutic injections performed by both professionals and non-professionals appear to be the predominant mode of HCV transmission and may account for up to 40% of all HCV infections worldwide (21,22). Supplies of sterile syringes may be inadequate or nonexistent; non-professionals often administer injections outside of a medical setting; and injections are often given to deliver medications that could otherwise be delivered orally. In addition to unsafe injection practices, lack of attention to appropriate cleaning and disinfection of equipment used in hospital and dental settings and blood transfusions from unscreened donors may also be important sources for HCV transmission.

In most low prevalence areas, illegal injection drug use is the predominant mode of transmission. Although transfusion- and transplant-associated HCV infections have been virtually eliminated through routine testing of donors (14, 22,23), outbreaks of iatrogenic transmission of HCV continue to occur associated with contamination of multiple dose medication vials and intravenous solutions by reuse of disposable needles and syringes (19).

4. Co-infection with HIV

Among the estimated 40 million persons infected with HIV worldwide, an estimated 2–4 million are chronically infected with HBV and an estimated 4–5 million are chronically infected with HCV. Several factors influenced these co-infection estimates, including geographic differences in the prevalence of chronic infection by age, the efficiency of exposures that account for most transmission, and the prevalence of persons at high risk for infection.

For example, in sub-Saharan Africa, heterosexual exposures are responsible for most HIV infections (4). Sub-Saharan Africa accounts for most (65%) HIV infections worldwide and has a high prevalence of chronic HBV infection because of perinatal and early childhood transmission patterns. HBV infections acquired at young ages are more likely to progress to chronic infections, resulting in a high prevalence of chronic HBV infection among the general population of adolescents and adults at risk for sexually-acquired HIV. Western Europe (and other

developed countries) account for a small proportion of HIV infections worldwide and have a low overall prevalence of chronic HBV infection because most native infections are acquired by adults who are substantially less likely to develop chronic HBV infection. Sexual (and injection drug use) exposures account for most HBV and HIV infections in developed countries, but among HIV-positive persons in some risk groups, the prevalence of chronic HBV infection may be ≥10-fold higher than the background prevalence. Among HIV-positive persons studied from Western Europe and the USA, chronic HBV infection has been found in 6–14% overall (24–28), including 4–6% of HIV-positive heterosexuals (26,27), 9–17% of HIV-positive MSM (24,26,27), and 7–10% of injection drug users (24–27) (Fig. 1).

For HCV infection, the geographic distribution of prevalence and primary mode of transmission relative to HIV are very different from those of HBV. The prevalence of chronic infection with HCV is estimated to be moderate (2–2.9%) in most of sub-Saharan Africa and low (<2.0%) in Europe and other developed regions (3). HCV is not efficiently transmitted by perinatal or sexual exposures, which are important modes of transmission for HBV and HIV. HCV is predominantly found in persons who have had large or repeated percutaneous exposures to infectious blood, such as persons who received unscreened blood or untreated clotting factor products and injection drug users (22). Although these persons are also at high risk for HIV, they account for a small proportion of the overall populations in most countries. Thus, in subpopulations of HIV-positive persons with history of injection drug use, 72–95% have been found to be co-infected with HCV (24,28–30); in HIV-positive persons who acquired their infection from sexual exposures, the prevalence of HCV co-infection has been found to be 8–35-fold lower, ranging from 1 to 12% among MSM (24,28–30) and 9–27% among heterosexuals (28,30) (Fig. 1).

Differences in infectivity between HBV, HCV and HIV have been observed in several settings. As indicated above, HBV and HIV are more efficiently transmitted perinatally and sexually than HCV. In the perinatal setting, maternal coinfection with HIV facilitates the transmission of HCV to newborns (31). MSM and long-term partners of persons with chronic infection have been shown to be at extraordinarily high risk for acquiring HBV and HIV infection. Although high-risk sexual behaviour (e.g. unprotected sex with multiple partners) is a risk factor for acquiring HCV infection, MSM are at no greater risk than heterosexuals, and long-term partners of persons with chronic HCV infection are rarely infected (22). Reasons for these differences are unclear.

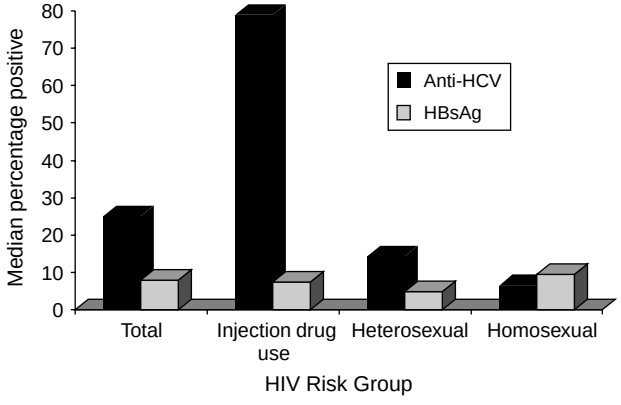

Fig. 1. Prevalence of chronic hepatitis B virus and hepatitis C virus infections in HIV positive populations by HIV risk group.

In the occupational setting, exposures to contaminated needlesticks among healthcare workers have demonstrated that HBV is 100 times more infectious than HIV and HCV is 10 times more infectious than HIV (22). In addition, experimental studies in animals have demonstrated that HBV and HCV can remain viable in dried blood on environmental surfaces at room temperature (32,33). Although HIV has been propagated in cell culture after drying at room temperature (34), it may not be infectious in humans. The difference in environmental survival capabilities of HBV and HCV compared with HIV may be one of the explanations for the more rapid acquisition of HBV and HCV infection among injection drug users, the association of HBV and HCV infections with sharing drug preparation equipment in addition to needles and syringes (35,36), and the more frequent episodes of iatrogenic transmission of HBV and HCV (18).

5. Summary

In summary, the characteristics of HIV infected persons differ according to the co-infecting hepatitis virus, and the epidemiology of the three viruses changes over time. In some Western European countries, 30–60% of infected sexual partners recently identified as sources for acute cases of hepatitis B and most HBV and HIV infected female commercial sex workers were from countries with high HBV and HIV prevalences, primarily sub-Saharan Africa. In Northern Europe, most injection drug users recently identified with chronic HBV infection were from countries with high HBV and HIV prevalences. Thus, ongoing surveillance or other systems are needed to monitor infection patterns for HBV, HCV, and HIV in order to ensure that prevention measures are targeted appropriately.

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