Human immunodeficiency virus and hepatitis C co-infection in sub-Saharan West Africa

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Accepted: 20 December 2005

ABSTRACT

Co-infection with human immunodeficiency virus (HIV) and hepatitis C virus (HCV) is becoming a major global problem, leading to increased morbidity and mortality in developed countries. Co-existence in sub-Saharan West Africa of a high prevalence of HIV and HCV, which share similar behavioural risk factors and modes of transmission, must be seen in the broader context of an emerging third epidemic of HIV and HCV co-infection, as many factors that may affect the spread of HIV and HCV co-infection are endemic in the continent, including host factors such as sexual behaviour, presence of other sexually transmitted diseases, female and male circumcision status, percutaneous and perinatal exposure, and poverty. This review examines the epidemiology, risk factors and transmission of HIV and HCV co-infection and draws attention to the possible emergence of an epidemic of HIV and HCV co-infection in the region.

KEY WORDS: Co-infection. Hepatitis C. HIV.

Introduction

Infection with human immunodeficiency virus (HIV)[1] and/or hepatitis C virus (HCV) represent a major epidemic globally.[2–5] Co-infection is characterised by a more rapid progression towards end-stage liver disease, leading to increased morbidity and mortality.[3] In some developed parts of the world up to 50% of patients with HIV are co-infected with HCV.[3] Increased focus on this problem has become necessary due to the increase in the lifespan of HIV-infected patients following the successful use of retroviral drugs.[6–11]

The epidemics of HIV and HCV co-infection found in some developed countries started with an HIV infection in the early 1980s among homosexuals and injection drug users, followed by an HCV epidemic in the early 1990s. This was followed almost immediately by a third epidemic: HIV and HCV co-infection. The factors[5] needed for the emergence of an epidemic of HIV and HCV co-infection are endemic in most sub-Saharan West African countries, and attention should be drawn to the dangers of such an epidemic.

Compared to those available in the industrialised countries, data on HIV and HCV co-infection in sub-Saharan Africa are very limited, despite the endemic nature of HIV infection and increasing reports of a high prevalence of HCV, in some cases with no identifiable risk factors.[12–14]

Available data predict sub-Saharan Africa to be saddled with the heaviest burden of an HIV/AIDS epidemic.[10] Similarly, the continent has been shown to have the highest HCV prevalence in the world (Table 1).[15] The co-existence of these two viruses, which share similar transmission routes, have precipitated fears of the emergence of HIV and HCV co-infection in the continent. The association of HIV/AIDS with tuberculosis[16] has already devastated the labour force of Africa and poses grave threats to countries already saddled with a heavy disease burden[15] and a limited health system.

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Epidemiology and natural history of HIV

The first cases of AIDS in sub-Saharan Africa were diagnosed in 1983,[17] a few years after AIDS was first diagnosed in the United States.[18] By the early 1990s the continent emerged as an endemic zone for HIV/AIDS.[10,18] This trend has been maintained, but a few countries have shown a progressive decline in incidence rates.[10]

The UNAIDS/WHO[10] report gave the estimated prevalence rate of HIV/AIDS for sub-Saharan Africa as 7.5–8.5%, which compares with prevalence rates of 0.2–0.4% for North Africa and the Middle East, 0.5–0.7% for North America and 0.3% for Europe (Fig. 1).

The report also indicated that 3.0–3.4 million adults and children were infected in 2003 alone, bringing the cumulative number of people living with HIV/AIDS in the region to 25.0–28.2 million. This report re-affirms the position of sub-Saharan Africa as the region with highest prevalence in the world.

A breakdown of the report also shows that some 11 million men, 15 million women and 3 million children are living with HIV/AIDS in sub-Saharan Africa. Thus, Africa has the highest number of infected women and children globally. This implies that sub-Saharan Africa, which accounts for less than 20% of the world's population, is saddled with more than 70% of the global HIV/AIDS burden.

Analysis of the data shows that seven southern African countries have prevalence rates above 20%: Botswana (38.8%), Lesotho (31%), Namibia (22.5%), South Africa

(20.1%), Swaziland (33.4%), Zambia (21.5%) and Zimbabwe (33.7%).[10]

In the sub-Saharan region of West Africa, HIV/AIDS prevalence rates for 14 out of the 21 countries in the region range from 0.3% in Senegal to 11.8% in Cameroon. Five countries have a prevalence above 5% but less than 10%: Burkina Faso (6.5%), Ivory Coast (9.7%), Nigeria (5.8%), Sierra Leone (7%) and Togo (6%). Prevalence in eight countries is below 5%: Benin (3.6%), Chad (3.6%), Equatorial Guinea (3.4%), The Gambia (1.6%), Ghana (3.0%), Guinea Bissau (2.8%), Mali (1.7%) and Senegal (0.5%).

Data for Cape Verde, Gabon, Guinea, Liberia, Mauritania, Niger and Sao Tome & Principe are not available.

Changing trend in HIV epidemiology

The gradual replacement of HIV-2 by HIV-1 has been reported in the region. Unlike HIV-1, infection with HIV-2 is associated with less immune suppression, slower disease progression and longer survival[19,20] and, because infected persons have a comparatively lower viral load, it has a lower transmission rate than HIV-1. HIV-2 infection is fairly well confined to the West Africa region,21,22 with nations such as Senegal, Mauritania, Cape Verde19 and Gambia[23] having prevalence rates ranging from 0.3% to 17%.24 The lower HIV/AIDS prevalence rate found in sub-Saharan West Africa may be due to the comparatively higher prevalence of HIV-2 in the region.

So far, this region of Africa may have escaped the level of devastation that has been inflicted on other regions by the HIV/AIDS disease burden, but, with a gradual decrease in HIV-2 infection and the increasing incidence of HIV-1 in the region,[19,23,25,26] the virus may soon make its presence felt. This changing trend may increase the HIV/AIDS disease burden of the region, taking into consideration the comparatively higher degree of virulence[24,27,28] and genetic diversity[26] associated with HIV-1 infection. Also, the gradual replacement of HIV-2 by HIV-1 may pose a major problem for vaccine design, as information on the genetic diversity of HIV, especially HIV-1, is vital for developing an effective vaccine.

Generally, differences in terms of geographical distribution, biological characteristics and major modes of transmission are associated with HIV subtypes. HIV-1 strains isolated in the USA and Europe are genetically different from strains isolated in Africa and Asia, with 20% or more variation seen in the envelope gene sequences between subtypes. It has also been shown that HIV-1 subtypes A, C, D and E are associated with heterosexual transmission and are found in sub-Saharan Africa, while subtypes A and B and subtype E are heterosexually transmitted in India and South-East Asia, respectively.

Intravenous drug users and homosexuals in North America and Western Europe are associated more with subtype B. Intravenous drug users and homosexuals in South East Asia and India are associated with subtypes B and C (Table 2).[29] Similarly, studies have shown that a higher proportion of HIV-1 with subtype C env can be transmitted in utero than HIV-1 with subtype A env, subtype D env, or a combination of both.[30] Therefore, there is a need for the initiation of community-based studies to keep track of the changing trends in HIV epidemiology and genetic diversity within sub-Saharan West Africa if suitable vaccines are to be designed and for their trials to be relevant and effective

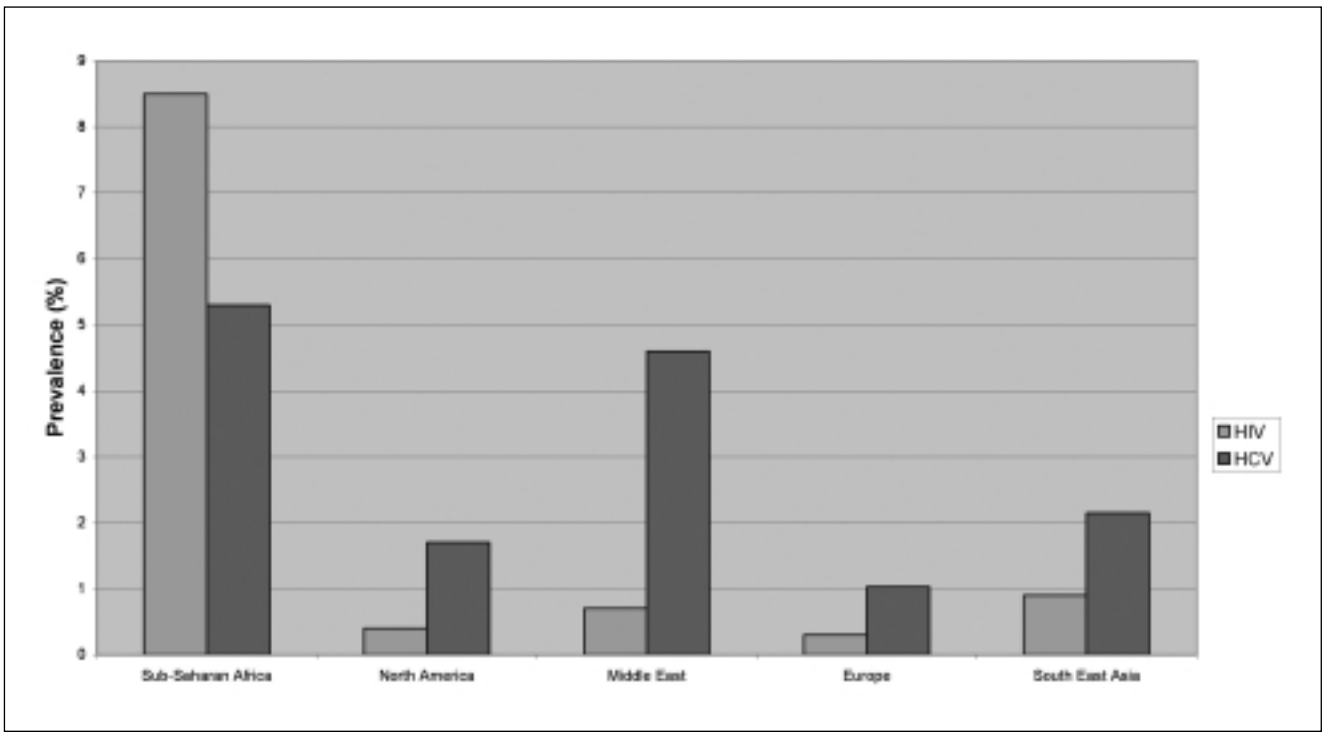

Fig. 1. Global distribution of HIV and HCV (HIV: UNAIDS/WHO 2003; HCV: WHO 1999).

Age and gender

Globally, young people are disproportionately affected by HIV and AIDS, and about half of all new HIV infections are in people aged 15–24 years.[15] At the onset of the HIV/AIDS epidemic in developed countries, up to 70% of those affected were homosexual or bisexual men;[31] however, with heterosexual sex now the principal mode of transmission, more women are becoming infected globally. In sub-Saharan Africa, HIV/AIDS occurs almost as frequently among females as among males, and this reflects the predominantly heterosexual route of transmission of the virus in the region.[10,32]

The UNAIDS report of 2002 revealed that more women than men are infected, with some countries having twice the number of women than men infected in all the 14 countries listed in the western sub-Saharan region. The epidemiological pattern emerging from some sub-Saharan African countries shows that, especially in polygamous settings, infection may cut across all age ranges and both sexes.[33] This is a major source of concern for epidemiologists and health planners.

Natural history and epidemiology of hepatitis C

Hepatitis C virus is an important bloodborne infection globally.[34,35] Its general benign nature in the acute stage, a tendency to become chronic in more than 70% of patients[34] and the lack of a preventive vaccine has made infection a major public health concern. This is exacerbated by the association of the virus with cirrhosis, end-stage liver disease and hepatocellular carcinoma.[36–38] Although, the incidence of HCV infection is believed to be falling,[34,38] this may be a feature of developed countries, as available data reveal Africa to be the continent in which HCV infection is most widespread.[39,40]

In developed countries, the extent of HCV infection came to light following the development of a diagnostic kit in 1989.[41,42] Diagnostic efforts have been reinforced since the emergence of the HIV epidemic, resulting in the almost risk-free transfusion of blood and blood products.[37,43] However, many developing countries have yet to implement diagnostic testing,[44] and routine screening for HCV is yet to become part of blood bank policy in some countries, making it difficult to curb the spread of infection.

In many sub-Saharan countries, data on HCV incidence or distribution are limited[44,45] and this has made it difficult for the tropical features of the disease to be fully understood.[46] In the early 1990s in Africa, prevalence of HCV was low and stable; however, this was based on selected evidence[47] and increased access to diagnostic facilities in some countries[4,12,43] does not support this assertion.

The current estimated global prevalence of HCV is 3%, which equates to approximately 170 million people.[2,4] Sub-Saharan Africa has a prevalence rate of 5.3%: prevalence in central Africa is 6%, West Africa is 2.4%, and southern and east Africa is 1.6 %.40 In comparison, prevalence in the Middle East is 4.6 %, South-East Asia is 2.15%, North America is 1.7% and Europe is 1.03% (Fig. 1). Highest prevalence of 20–30% is reported in Egypt,[39] with nearly all cases affected by type 4a.[48]

Table 1. HIV and HCV prevalence rates in sub-Saharan West Africa.

Country	% HIV-infected	Source	% Anti-HCV	Source
Benin	3.6	UNAIDS 2002	1.50*	4
Burkina Faso	6.5	UNAIDS 2002	‡	
Cameroon	11.8	UNAIDS 2002	12.50*	4
Cape Verde	‡			
Chad	3.6	UNAIDS 2002	4.80*	4
Cote d'Ivoire	9.7	UNAIDS 2002	3.3	5
Equatorial Guinea	3.4	UNAIDS 2002	1.7	80
Gambia	1.6	UNAIDS 2002	3.0	49
Gabon	2%†	Bertherat *et al*., 1998	6.50*	4
Ghana	3.0	UNAIDS 2002	5.40*	4
Guinea Conakry	6.7%†	Ruggieri *et al*., 1996	10.7*	4
Guinea Bissau	2.8	UNAIDS 2002	1.1	
Liberia	‡			
Mali	1.7	UNAIDS2002		
Mauritania	1%†	Lo et al., 1999	0.3*	81
Niger	3.2%†	Mamadou *et al*., 1997	2.5*	4
Nigeria	5.8	UNAIDS 2002	1.4*	4
Sao Tome and Principle		‡		
Senegal	0.5	UNAIDS 2002	2.9*	4
Sierra Leone	7.0	UNAIDS 2002	2.0	13
Togo	6.0	UNAIDS 2002	3.3*	4

*WHO (1997); †No data available in UNAIDS 2002 report; ‡Data unavailable or unrelated.

In The Gambia it is reported that an HCV prevalence of 3% is found among an apparently healthy population.[49] In Sierra Leone, prevalence of 2% among children aged 6–12 year with identifiable specific risk factors is reported.13 Among blood donors, prevalences of 17%, 1.4%, 1.8%, 12.3%, and 0.9% have been reported in Rwanda,[45] Benin,[50] Kenya,[51] Nigeria[52] and Ghana,[53] respectively. Distribution of HCV is related to socio-economic status, which gives rise to considerable geographic and temporal variation in its incidence and prevalence.[2]

A World Health Organization report 15 on the global distribution of HCV showed that of the 21 countries in the western sub-Saharan region, data were only available in nine. However, information from another seven countries has been obtained for this review by searching PubMed, but only recently published studies that target populations at low risk of acquiring the infection were considered for inclusion. Information from Burkina Faso, Cape Verde, Liberia, Mali and Sao Tome was either not available or was not representative of the low risk groups.

Analysis of this data show that four countries had prevalence rates above 5%: Cameroon (12.50%), Guinea Conakry (10.7%), Gabon (6.5%) and Ghana (5.4%). Five

countries had prevalence rates above the global level: Chad (4.8%), Ivory Coast (3.3%), The Gambia (3.0%), Senegal (3.0%) and Togo (3.3%). Seven other countries had prevalence rates that ranged from 0.3% in Mauritania to 2.5% in Niger.

Average HCV prevalence for 16 of the countries in the region from which data are available is 3.9%. However, most of the data is up to eight years old, so current prevalence may be considerably higher.

Genetic diversity and distribution of HCV

Variation in HCV according to geographical regions may influence the clinical outcome of the disease,[54] but genetic diversity and distribution of HCV genotypes in sub-Saharan Africa is poorly documented. One report suggests a high level of diversity among HCV genotypes 1 and 4, and also provides evidence that these genotypes originated and diversified in west central Africa before spreading to other regions.[55]

In order to design vaccines and treatment strategies, more work needs to be done to improve available data on the genetic diversity and distribution of HCV in the region. This is particularly important because some correlation has been found between HCV transmission routes, patient age,[56] and virus genotype in developed countries.

For example, blood donors and those with chronic hepatitis in Western Europe and North America are affected predominately by types 1a, 1b, 2a, 2b and 3a, whereas type 1b is more common in southern and eastern Europe. Similarly, type 1a dominates in haemophiliacs in Japan. Sadly, information about the genetic distribution of HCV in most sub-Saharan countries is incomplete.

Epidemiology of HIV and HCV co-infection

In developed countries the epidemiology of HIV/AIDS has changed, from an infection considered to be exclusively of homosexuals[31] to one that affects all other groups.[57] Similarly, HCV has shifted from being transmitted primarily by nosocomial and other iatrogenic routes,[58] to needle sharing by intravenous drug users. As HIV and HCV have similar transmission routes, the epidemiological change in infection trends means that most people infected with HIV in the developed countries are also infected with HCV.

In the USA for example, it is estimated that 60–90% of HIV-positive haemophiliacs and 50–90% of HIV-positive iv drug users are co-infected with HCV.59 Similarly, 60% of iv drug users, 22% of AIDS cases in men and 42% of AIDS cases in women account for 60% of newly acquired cases of HCV infection.[59,60] Thus, HIV and HCV co-infection has become the major cause of morbidity and mortality among HIV-infected patients.[44, 61]

Available data on co-infection in sub-Saharan Africa have shown an epidemiological profile entirely different from that of the developed world. In what probably is the first major study, in 1994, on co-infection to emerge from sub-Saharan Africa, 4593 serum samples were collected (cohort age range: newborn to 49 years) as part of a household community survey in Addis Ababa for HCV antibodies using a third-generation enzyme-linked immunosorbent assay (ELISA) test kit.[62] Antibody prevalence rate was 4.5% among HIV-positive individuals and 0.8% among HIV-negative persons. The HCV-positive rate in HIV-positive and HIV-negative antenatal cases was 2.9% and 0.8%, respectively, and among HIV-positive and HIV-negative sex workers it was 5.3% and 1.3%, respectively. Another study conducted in Cote d'Ivoire on samples collected in 1995/96 from 2198 women attending gynaecology clinics in Abidjan reported an HIV and HCV co-infection rate of 3.3%.[5]

These studies carried out on samples collected over a decade ago confirmed the existence of low-level HIV and HCV co-infection in the region. Although limited data have been reported on HIV and HCV co-infection in the region, existence of an HCV prevalence of 3.9% in the region a decade ago, alongside increasing HIV prevalence, should be considered a major epidemiological problem that needs to be addressed urgently. An in-depth population-based epidemiological study is needed to address this issue.

Risk factors and transmission of HIV and HCV

Transmission routes for HIV and HCV are well established,[38,63,64] with heterosexual sex[65] and intravenous drug use the primary routes, respectively.[66] However, nosocomial transmission still poses a major threat[67,68] for both infections, especially in developing countries. Although there remains some controversy about the heterosexual transmission of HCV,[69] available evidence confirms the sexual transmission of HCV at a lower level of efficiency.[70] Similarly, in subjects in whom sex is the only risk factor for HCV transmission, the presence of HIV may enhance its transmission.[14]

Studies in some parts of Africa report high HCV prevalence without established routes of transmission. In the Central African Republic, a country with an estimated HIV/AIDS prevalence of 12.9%, Fretz and colleagues found an HCV rate of 2.8%.[71] Another report showed an HCV prevalence of 17.1% in a southern Cameroon village, which increased significantly with age ($P<0.05$), suggesting iatrogenic rather than continuous exposure.[5] In Cote d'Ivoire, HCV prevalence of 3.3% among women attending gynaecology clinics in Abidjan was reported; however, the authors concluded that it was not explained by sexual transmission.[5]

Some studies show that male and female circumcision, along with other traditional practices that involves blood letting, can enhance the transmission of HIV and other viruses,[72] while high levels of promiscuity[73] and prostitution are all major contributors to the spread of HIV and other sexually transmitted diseases in the region. These reports indicate that the transmission and prevalence of HCV, like HIV, in sub-Saharan Africa may be related to each community's cultural and traditional practices.[33] Thus, there may not be a generalised transmission pattern and the search for other transmission routes for HCV should include community-based longitudinal studies. Such studies should look at individual community cultural practices and taboos, which may uncover iatrogenic causes such as reuse of instruments and objects during rituals and other activities such as male and female circumcision, scarification, tattoos and body piercing.

Owing to limited resources, many sub-Saharan African countries have yet to put in place effective blood screening practices to address the problem of bloodborne pathogens, including HCV.[44] Furthermore, inadequate hospital supplies may lead to the use of unsterile healthcare equipment, reuse of disposable needles and syringes[42,74] and of disposable gloves. However, currently there is little data on nosocomial transmission of HCV in most countries in Africa.

Efficiencies of HIV and HCV transmission

Although HIV is transmitted predominantly by heterosexual sex in sub-Saharan Africa, which is among the least efficient routes of transmission,[75] this accounts for 60% of global HIV/AIDS cases.[32] Transmission efficiency via blood transfusion, iv drugs use and needlestick exposure is 90–95%, 0.5–1% and <0.5%, respectively. Perinatal transmission was 20–40%32 prior to the availability of antiretroviral drugs.

Similarly, HCV transmission efficiency following transfusion of a unit of HCV-infected blood is estimated at >90%,[76] while perinatal HCV transmission efficiency is 1–7%, needlestick injury is 2–8%[77] and sexual contact is <1%.78 Furthermore, the estimated risk factor for HCV in HIV co-infection is 1–20% and <4% for perinatal transmission, while the risk associated with needlestick injury is unknown[76] (Table 3). Collectively, these latter routes account for some 25% of global HIV/AIDS cases.[32]

Some reports have shown that the major source of HCV infection globally is iv drug use, while sex is connected with a prevalence rate of 15%, although this is controversial. Blood transfusion accounts for 10% while others such as nosocomial, iatrogenic and perinatal account for 5%, and unknown sources account for 10% (Fig. 2). Generally, transmission efficiency is determined by the amount of virus in a body fluid and the type and extent of contact.[79]

Although few studies have evaluated the risk of nosocomial transmission of HIV and HCV, other than by blood transfusion, in the developing world, the higher transmission efficiency of HCV after percutaneous exposure to blood or other infected body fluid[68,74] means that this should be reviewed as a potential route of HCV transmission. Also, concern should be raised about the use of gloves as a means of patient-to-patient transmission, in addition to the recognised sources such unscreened blood and the reuse of needles and syringes.

Diagnosing HIV and HCV

Estimating the long-term effects of HIV and HCV co-infection can only be done with certainty when the epidemiology of the disease is known. Although some studies show the economic cost of HIV infection in sub-Saharan Africa to be colossal,[80, 81] such data do not exist on HIV and HCV co-infection. A press release by WHO/AFRO in 2001[82] indicates that over 75% of blood units transfused in Africa are not tested for HIV, while more than 80% of the countries in the region do not test blood units for HCV before transfusion. Diagnosis of HIV and HCV co-infection in the region is still handicapped by several factors in the region. These include: ignorance, self-medication, cultural beliefs and traditional practices; and finance, manpower, equipment and supplies.

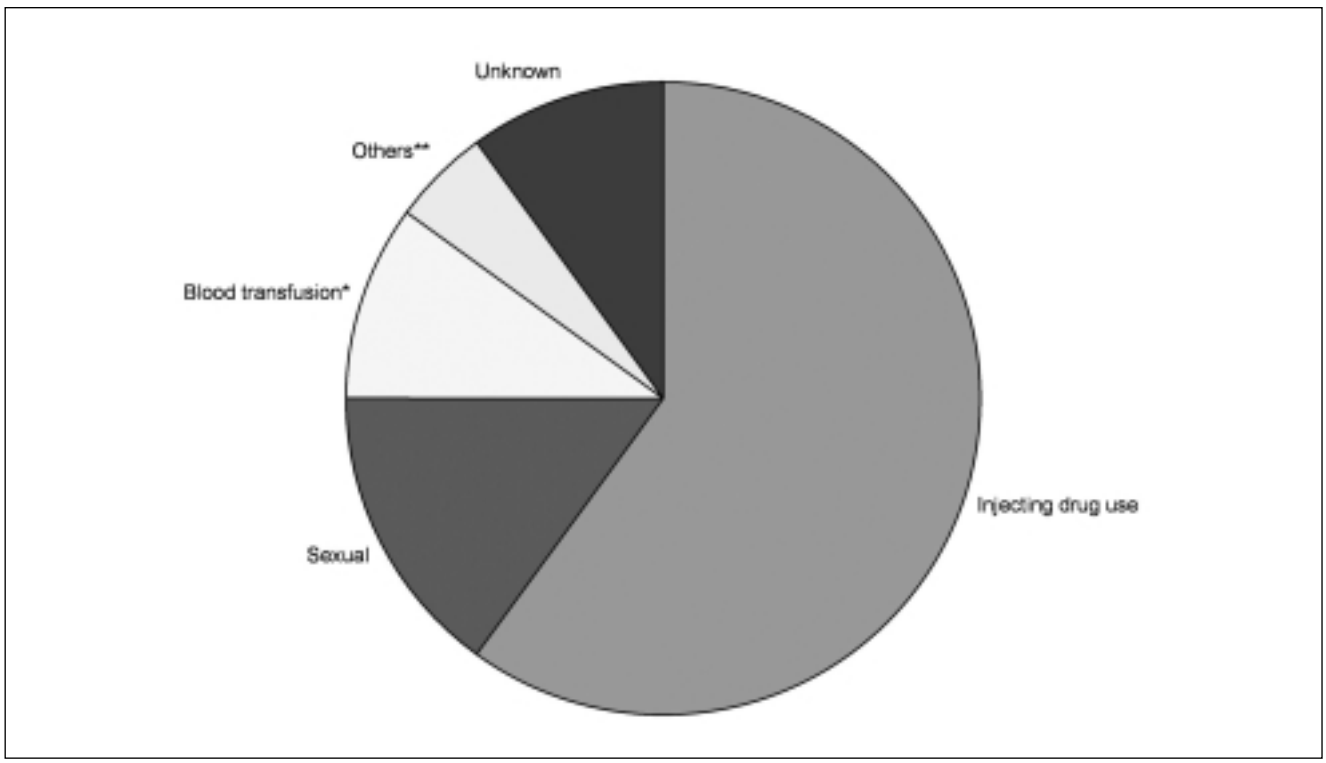

Fig. 2. Sources of HCV infection (CDC).

Table 2. Geographical distribution of HIV-1 subtypes and their predominant mode of transmission.

HIV-1 subtypes	Predominant mode of transmission	Where found
A, C, D and E	Heterosexual	Sub-Saharan Africa
A, B and C	Heterosexual	India
E	Heterosexual	South-East Asia
B	Homosexuals and IDUs	North America, Western Europe and South-East Asia
B and C	Homosexuals and IDUs	India

IDUs: intravenous drug user
Source: www.nacoonline.org/publication/7.pdf

Table 3. Efficiency of transmission of HIV and HCV following different types of exposure.

Exposure	Estimated risk (%)			
	HIV	Ref	HCV	Ref
Blood transfusion	90–95	32	>90§	76
Perinatal	20–40*	32	1–7	77
Sexual contact	0.1–1†	77	<1	77
IDU	0.5–1	32	0.0067‡	78
Needlestick	<0.5	32	2.7–6	79

*Prior to availability of antiretroviral drugs.
†Unprotected heterosexual act.
‡Per injection.
§Per unit of infected blood transfused

Ignorance, self-medication, cultural beliefs and traditional practices

Self-medication[83–85] as a result of the lack or near absence of medical facilities, ignorance or poverty, attitudes of healthcare, providers, cultural beliefs and traditional practices contribute not only to the HIV/HCV disease burden in sub-Saharan Africa but also to the problems associated with their diagnosis. Traditional medicine practitioners are often the first choice for treatment,[83,84] with orthodox medicine only considered when all else fails. This is due mainly to ignorance, cultural beliefs and poverty.[85]

Few countries in the region have formulated an appropriate official policy on the use of traditional medicine,[87–89] and even in those where such policies do exist they may not be effective.[86] Some countries have policies that discourage traditional medicines,[86] while others are supportive.[87] However, it is unlikely that traditional medicine practitioners recognise HIV/AIDS or HCV as specific disease entities.

Given the high patronage of traditional medicine in the region,[83,84] its non-integration with orthodox medicine and the fact that traditional medicine is embedded in local cultures and beliefs, there is urgent need for it to be integrated into the formal system of healthcare delivery.

Finance, manpower, equipment and supplies

Decisions about what to screen for in most diagnostics laboratories in sub-Saharan African often have to be weighed against a range of other health problems competing for limited resources, and this means that HCV diagnosis is regarded as a low priority in many countries.[81,90,91] Other identified constrains include the inadequate supply of reagents, irregular power supply and a lack of equipment.[81] These problems have contributed to inadequacies in HCV screening facilities in many countries in the region.[44,81]

Similarly, even where simple diagnostics tests for HIV are available, facilities for the diagnosis of HIV in infants[92,93]and for HCV may be lacking or simply may not exist. The standard method for the diagnosis of HIV in babies is a polymerase chain reaction (PCR) technique, but such methodology is limited in most sub-Saharan African countries. Thus, early accurate diagnosis of HIV in infants remains a major problem.

Conclusions

Co-infection with HIV and HCV is a major cause of morbidity and mortality in several developed countries. A high prevalence of this co-infection in sub-Saharan West Africa makes the region a potential source of an emerging epidemic. Identifying risk factors and routes of transmission is essential for effective intervention. Routine blood screening for HIV and HCV should be considered mandatory for all blood banks in the region, and all patients with HIV should be tested for HCV to ensure early identification.

Epidemiology of HIV, HCV and co-infection may show important differences between developed and developing countries. Caution should be exercised in extrapolating findings from developed countries to ethnic populations in sub-Saharan Africa, which may show an entirely different pattern in the natural history of HCV infection. Thus, community-based longitudinal studies should be initiated to evaluate the distribution and genetic diversity of HIV and HCV in the region as a means of facilitating vaccine design and trials. Such studies must also evaluate local cultural and traditional practices that may favour or enhance the transmission of infection. □

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