3

HIV Prevention Needs Epidemiological Data

Anatole Tounkara et al.*
SEREFO HIV/TB research and Training Center, University of Bamako
Mali

1. Introduction

Infection with human immune deficiency virus (HIV) is a challenging problem to public health, because it often involves long term treatment with advanced drugs to prolong survival of patients diagnosed with the infection. As an important public health preventive measure, it is necessary to give an HIV-infected individual antiretroviral therapy (ART). This measure facilitates the reduction of the risk of the infected individual from transmitting the virus to others by reducing the viral load in that person. But often, the drug regimens used are surrounded by such questions as the best timing for initiation of therapy as well as benefits and risks associated with delay or early treatment. As a result health caregivers for HIV need to have a continuous update of their knowledge and skills on HIV care and counseling so that they can manage and support individuals with HIV/AIDS with the best and most effective strategy. One way to develop an effective preventive response against HIV is to understand how the infection spreads and the factors that contribute to new infections.

Data from epidemiological studies indicate that, worldwide the prevalence of HIV increased from 29 million in 2001 to 33.4 million in 2008. Similarly, other opportunistic infections such as tuberculosis, cryptococcal meningitis as well as the drug-resistant forms of these diseases altogether add up to make the management of HIV a complex activity. Whereas the incidence is declining in many parts of the world due to access to effective drug regimens, the trend in developing countries has stabilized or slightly increased. Available data from 11 West African countries indicate that national prevalence of HIV/AIDS had been stable in these countries ranging from <1% in Senegal and Niger, to 6.7% in Guinea Bissau. With the exception of Senegal and Ghana, the prevalence rates of these countries were higher in the urban than in the rural areas. The spread of HIV in this region is of great concern to many organizations and governments because of predictions of its increase, yet data are scarce and not regularly revised to reflect current estimates for the countries in this region. In addition, there is the presence of both HIV-1 and HIV-2 in this region. Though more importance is placed on the former than the latter because it is thought to be more easily transmissible while conflicting reports have been shown for the later regarding its

*Abdulrahman S. Hammond[2], Bassirou Diarra[1], Almoustapha Maiga[1], Yaya Sarro[1], Amadou Kone[1], Samba Diop[1] and Aboubacar Alassane Oumar[1]
[1]*SEREFO HIV/TB research and Training Center, University of Bamako, Mali*
[2]*SAIC Frederick, Maryland, USA*

protection of HIV-1 and a lower progression to disease. There is great enthusiasm by many stakeholders in establishing preventive measures to control increase in HIV-1 in the region, however, not much is done about estimation of transmission dynamics and monitoring of coverage of interventions.

In Mali, estimates from 2006 indicated that the overall prevalence of HIV was 1.3% in the general population, 2.2% among young adults (between the ages of 15 and 30), and 35.3% among sex workers (Samake, 2006). The main factors associated with HIV infection in Mali are limited access to treatment and extreme poverty. However, other factors such as poor health conditions, low literacy levels and certain cultural practices like male dominance of women, low condom use, and a relatively high prevalence of sexually transmitted diseases, all contribute to HIV transmission in Mali. Here, we review some of the preventive methods adopted for the management of HIV in Mali. Our review includes current epidemiological data in the general population and the different forms of circulating HIV strains as well as HIV transmission risk behaviors among patients diagnosed with HIV infection in Mali. We also discuss progress made with effective distribution of drug regimens and throw light on the debates of when to start therapy as well as the benefits and demerits of these measures.

2. Epidemiology

2.1 Overview of HIV infection in Mali

Mali is a landlocked country situated in West Africa with a size of 1,241,248 Km^2 and a population of approximately 14.5 million inhabitants. The country is divided into 8 administrative regions with Bamako as the capital. The north stretches deep into the Sahara and is inhabited mainly by the Tuaregs and the nomadic Fulani tribes. Two major rivers, Niger and Senegal, flow through the southern region. A number of countries share border with Mali and includes Algeria in the north, Niger in the east, Burkina Faso in the south-east, Cote D'Ivoire and Guinea in the south, and Mauritania and Senegal in the west. Distribution of HIV prevalence varies from one region to another. Based on two surveys the highest recorded prevalence is observed to be in the Bamako region, where majority of inhabitants live.

A report of HIV/AIDS was first made in 1985 in Mali. In 2001, the Demographic and Health Survey indicated a prevalence of 1.7% among adults (Pichard, 1988; Ballo, 2001). This survey hinted that the prevalence in the general population could increase three-fold if appropriate preventive measures are not put in place to curtail the spread of the infection. Consequently, with a strong commitment from the government a National AIDS Program (NAP) was formed and by 2006 the rate had decreased to 1.3%. The NAP was again restructured in 2002 by which time rates of HIV infection was higher among young women (mostly pregnant women with prevalence ≤5%) between the ages of 25 to 29 years than young men. Similarly, among the 30-34 years age group, women had 2.2% prevalence against 1% prevalence for men. Table 1 shows the distribution of HIV prevalence in Mali between the regions. Overall, prevalence is higher in the urban areas (1.3%) than in the rural (0.6%). Though there are poor records of transmission and prevalence rates, the survey in 2006 showed that sex workers were the highest risk group with 35.3% rates, followed by young street vendors (5.9%), drivers (2.5%), while casual workers and the unemployed youth shared the same rate (2.2%) (Samake, 2006).

It is worthy of mention that Mali is a poor country with about 70% of the population in extreme poverty. In addition, a similar proportion, mainly women are illiterate. A number of socio-cultural practices such as excision and tattooing are commonly found among the

population. The 2006 sentinel study indicated that there was early onset of sexual activity among young women and in addition there is generally low condom use by young males between the ages of 15 and 24 years. These together posed a risk factor for infection among the young population in which 2 out of 3 did not believe in the existence of HIV/AIDS (Samake, 2006).

ADMINISTRATIVE MAP OF MALI

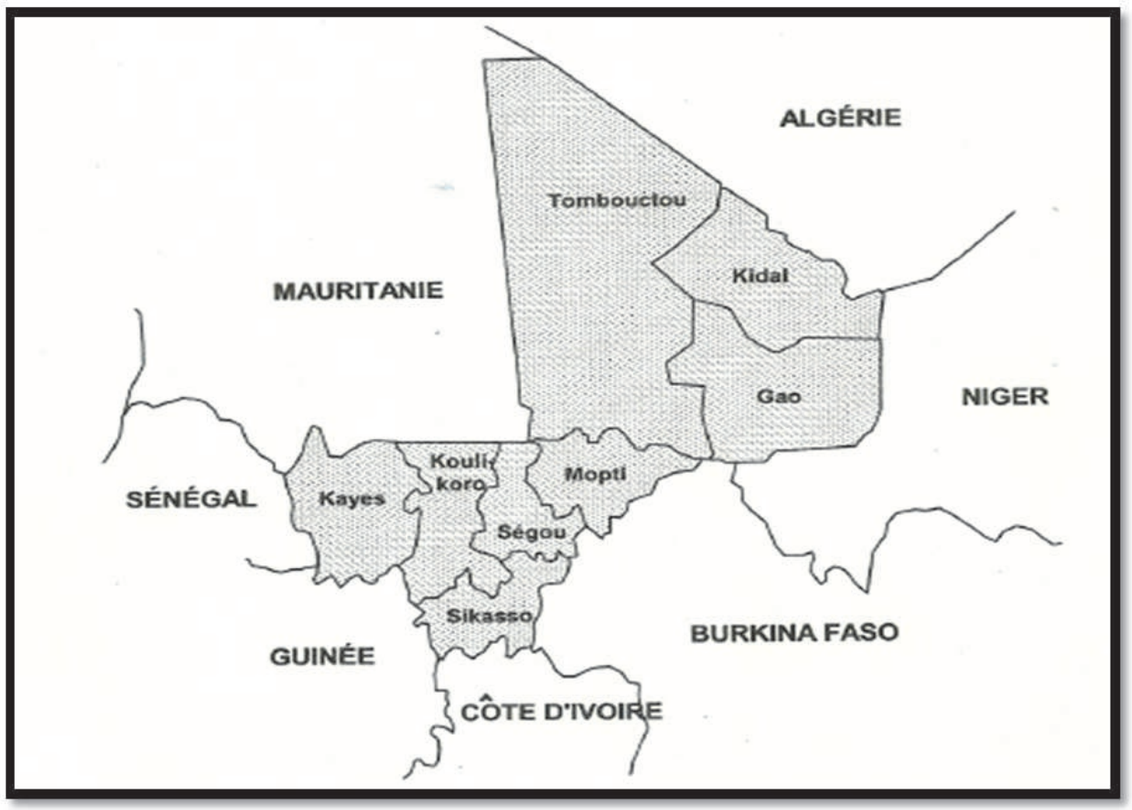


Fig. 1. Map of Mali showing the 8 administrative regions (Samake, 2006).

Regions of Mali	Prevalences	
	2001	2006
Kayes	**1.9**	**0.7**
Koulikoro	**1.9**	**1.2**
Sikasso	**1**	**0.6**
Segou	**1.9**	**1.3**
Mopti	**1.4**	**1.4**
Gao	**0.7**	**1.1**
Tombouctou	**0.7**	**0.5**
Kidal	**0.7**	**0.6**
Bamako	**2.5**	**1.9**

Note: This table shows the differences between the two national surveys of HIV prevalence in the different regions of Mali. As can be seen HIV prevalence decreased in the period 2001 to 2006.

Table 1. HIV prevalence in 2001 and 2006 from different administrative regions of Mali.

In 2001, the Malian initiative of access to antiretroviral therapy (IMAARV) was created. This initiative organizes, implements and follows up antiretroviral therapy in patients infected with HIV. The most important effort of the Malian government was to make free the distribution of antiretroviral drugs for all patients including diagnosis and follow up. This measure allowed the acquisition of regular data from different groups working in HIV field.
Thus, the data presented in this chapter represents those from different groups working in Mali, and includes epidemiological data from the Malian health system and research reports.

2.2 HIV prevalence among the educated & non-educated folk

Although HIV epidemic is related to certain behaviors that exposes an individual to the virus and subsequently increases the risk of the individual to infection, unsafe behaviors are the main contributing factors to transmission of HIV in Mali. For instance, condom use among young males between the ages of 15 and 25 is around 30% and 14% for young women. Similarly, condom use is low among military personnel, truck drivers and vendors of all kinds.
Given that knowledge about HIV is important in identifying and better understanding populations most at risk for HIV infection, the national control program embarked upon different strategies and campaigns to assess knowledge and behavior of students about HIV regarding the different routes of transmission. In the study that also assessed the prevalence and predictors of HIV infection among 950 high school and University students in three regions of Mali, namely, Bamako, Sikasso and Koulikoro, it was observed that the prevalence rate was respectively 3.6, 1.8, and 3.4%. Overall prevalence of HIV was 3.1% and both HIV-1 and 2 were circulating in the schools, although there was more HIV-1 (93.1%) than HIV-2. The study however, did not observe any association between HIV status and the following predictors: age, sex, marital status, religion, education level, ever had intercourse, current sexual partner, condom use at last sexual intercourse, casual sex and study site. By regression coefficient (1.25; $p< 0.01$) the study showed that the main significant predictor of HIV infection was knowledge of route of infection (White, 2009). Thus it demonstrated that the most feasible strategy for slowing down the HIV/AIDS epidemic is education towards risk reduction and prevention of infection. It is not known yet whether there have been follow up studies to understand why the students who had knowledge of the route of transmission of HIV infection were more at risk so that better and more effective strategies can be designed to prevent future occurrence.

2.3 HIV Infection in jail

Few studies were conducted in the Malian prisons. This is particularly due to the strict government regulations that protect the occupants of these prisons. The prisoners are known to be at high risk for HIV infection because of unsafe behaviors in these places (Pichard, 1988). Thus knowledge of prevalence in this group has relevant impact on designing strategies for prevention in these areas. To this end, some studies have looked at attitude, risk behaviors and knowledge of HIV within jail population, and noted that most inmates of a jail had limited knowledge of the definition of HIV/AIDS. Only 2.7% knew that AIDS is an Acquired Immunodeficiency Syndrome and can be transmitted through body fluids and by sex. The study also showed limited knowledge of routes of transmission for both HIV and Sexually Transmitted Diseases (STDs), and only 7.5% of the study population knew their HIV status (TCHOUZOU, 2008).

Recommendations from this study led the national program against HIV/AIDS to initiate large campaigns in 2006, regarding the routes of transmission of HIV in order to educate people in different communities including prisoners. Topics covered in these campaigns included sexual transmission, intravenous drug use, mother-to-child transmission of HIV, risks from blood products and transfusion, organ donor or tissue transplantation as well as risks of occupational exposures to the virus. Similarly, there is a need to conduct follow-up studies to determine the prevalence of HIV so that improved recommendations can be made for implementation, particularly in the jails.

2.4 HIV prevalence among blood donors

Whereas HIV overall prevalence in Mali is currently 1.3%, prevalence among blood donors is 2.6% (Diarra, 2009). Estimates from the National Center of Blood Transfusion (Centre National de Transfusion Sanguine [CNTS], Bamako, Mali) indicate that this rate had risen from 3% in 1999 to 4.5% in 2009 (Tounkara, 2004; Tounkara, 2009) and decrease to 2.6% in 2007 (Diarra, 2009). Young adults (between 18 and 25 years) accounted for 41% of overall blood donors. It is important to note that, 1.13% of the blood donors with HIV were also co-infected with Hepatitis B virus (HBV) (Table 2). Of these, 88.5% are men (over 25 years of age), while young adults make up 43%. About 80% of the blood donors from the cohort at CNTS were recruited from family members of patients who need blood transfusion. From this cohort some studies have shown that majority of the HIV seropositive individuals had thrombocytopenia, with a platelet count lower than 150 x 10^3/mm^3 (Tounkara, 2004). Compared to HIV seronegative individuals, the HIV infected had longer bleeding time, a diminution of the rate of prothrombin, and an elevated partial time for thromboplastin. Taken together, these data suggest a modification of hemostasis over the course of HIV infection (Tounkara A, 2004). Also, a proportion of blood donors were found to have human cytomegalovirus (HCMV). Among these, 89% were AIDS patients, 71% were HIV-infected and 58% were uninfected with HIV. About 40% of the blood donors co-infected with HIV and HCMV also had pneumonia compared to those infected with only HIV (Maiga, 2003; Tounkara, 2004).

	HBV Status		
HIV Status	Positive, n (%)	Negative, n (%)	Total, n (%)
Positive	131 (1.13)	387 (3.34)	518 (4.47)
Negative	1591 (13.73)	9483 (81.80)	11 074 (95.53)
Total	1722 (14.86)	9870 (85.14)	11 592 (100)

Abbreviations: HBV, hepatitis B virus; HIV, human immunodeficiency virus; n, number of donors; %, percentage of the specific cell based on the total number of donors (11 592).
Note: This table represents HIV and HBV infection alone as well as the prevalence of co-infection among Malian Blood donors.

Table 2. HIV/HBV Coinfection Frequency among Blood Donors in Mali

Studying HIV prevalence among blood donors will help to refine strategies used in recruiting blood donors, and significantly reduce HIV transmission in the general population.

2.5 Circulating recombinants forms of HIV in Mali

A lot of interest has been generated by the scientific community in seeking to understand the range of variability of HIV so that the spread of an epidemic can be tracked between different population and places, as well as develop strategies to control the virus. Firstly, HIV is thought to be the most variable virus, and its clinical characteristics alone are not sufficient to explain the outcomes of infection. In addition, it has subtypes with distinct geographic distribution and recombination can occur between and within subtypes (Korber, 2003). Thus creating a further increase in the genetic diversity in many parts of the world and thereby a complex challenge to control. As a result, the role of genetic variability in HIV infection has received extensive consideration both for understanding of the natural history of the disease and for developing strategies for control of the virus. Currently 9 subtypes have been identified worldwide in the HIV-1 group M (A, B, C, D, F, G, H, J and K). Viruses E and I in the envelope are recombinant strains (Peeters, 1999). In 2009 estimates showed that approximately 2.6 million [2.3 – 2.8 million] new infections were due to HIV-1 subtype non-B, and these were predominantly among infected individuals in the Americas, Western Europe, and in Australia (Report 2010 of UNAIDS). More than 50% of HIV infections worldwide are associated with the HIV-1 subtype C, with South Africa having the highest majority, while subtypes A and D are commonly found in East Africa. The prevalence of recombinant forms of HIV has been increasing, and in Europe it rose from 17% during the period 1996-1999 to 28% in the period 2000-2003 and again to 35% in 2006-2009. The most common recombinant strain in circulation in some regions of Africa and West Asia is the HIV-1 Circulating Recombinant Form (HIV-1 CRF).

A number of studies have characterized subtypes in Mali and other West African states, and have noted that the recombinant CRF02_AG is the main HIV-1 infecting strain in this region. Sequencing analysis has revealed that early failures to Triomune ® (d4T/3TC/NVP) in adults occurred because the viruses in circulation were recombinant CRF02_AG (Marcelin, 2007). Recent primary drug resistance studies conducted in Mali (in Bamako and Segou) on 198 samples obtained from ARV-naive patients showed CRF02_AG to be the most prevalent strain, with respectively 70.5 and 72% occurring in 2005 and 2006 (Derache, 2008). A second recombinant strain was CRF06_cpx with 19.5% and 11% infections respectively occurring in the same period. Other subtypes and recombinants in circulation were also found, but with a lower prevalence in these two years. Overall, there was a greater genetic diversity in the year 2006 compared to 2005. Indeed, in 2005, two pure subtypes (C and G) and a recombinant (CRF01_AE) were found, while in 2006, three pure subtypes (A, F2 and G) and 3 recombinants (CRF01_AE, CRF09_cpx and CRF18_cpx) were identified (Derache, 2007). The prevalence of CRF02_AG appeared to be stable, while that of CRF06_cpx decreased, giving way to other subtypes, including CRF09_cpx and CRF18_cpx which are new strains in Mali. The recombinant CRF09_cpx, is a mosaic virus from different subtypes (A, F and G), and although it was first described in 2004, in West Africa, it is now the most predominant recombinant strain in the region. This recombinant appears to have structural similarities as well as important genetic distances like the first CRF02_AG isolated (McCutchan, 2004). As for the recombinant CRF18_cpx, this was first identified in 2005 in Cuba, but now, seems native to Central Africa. Indeed, it consists of various segments from the CRF13_cpx, CRF04_cpx and 36 other viruses, is predominantly found in Central Africa (Thomson, 2005). Similarly, a recent study in Mali found a subtype namely, CRF05_DF (Maiga, 2010). This subtype, CRF05_DF, was first described in Belgium in 2000 from a patient linked to the Democratic Republic of Congo (DRC) (Laukkanen, 2000). Thereafter, Casado and colleagues identified another strain in 2003 in the DRC (Casado, 2003).

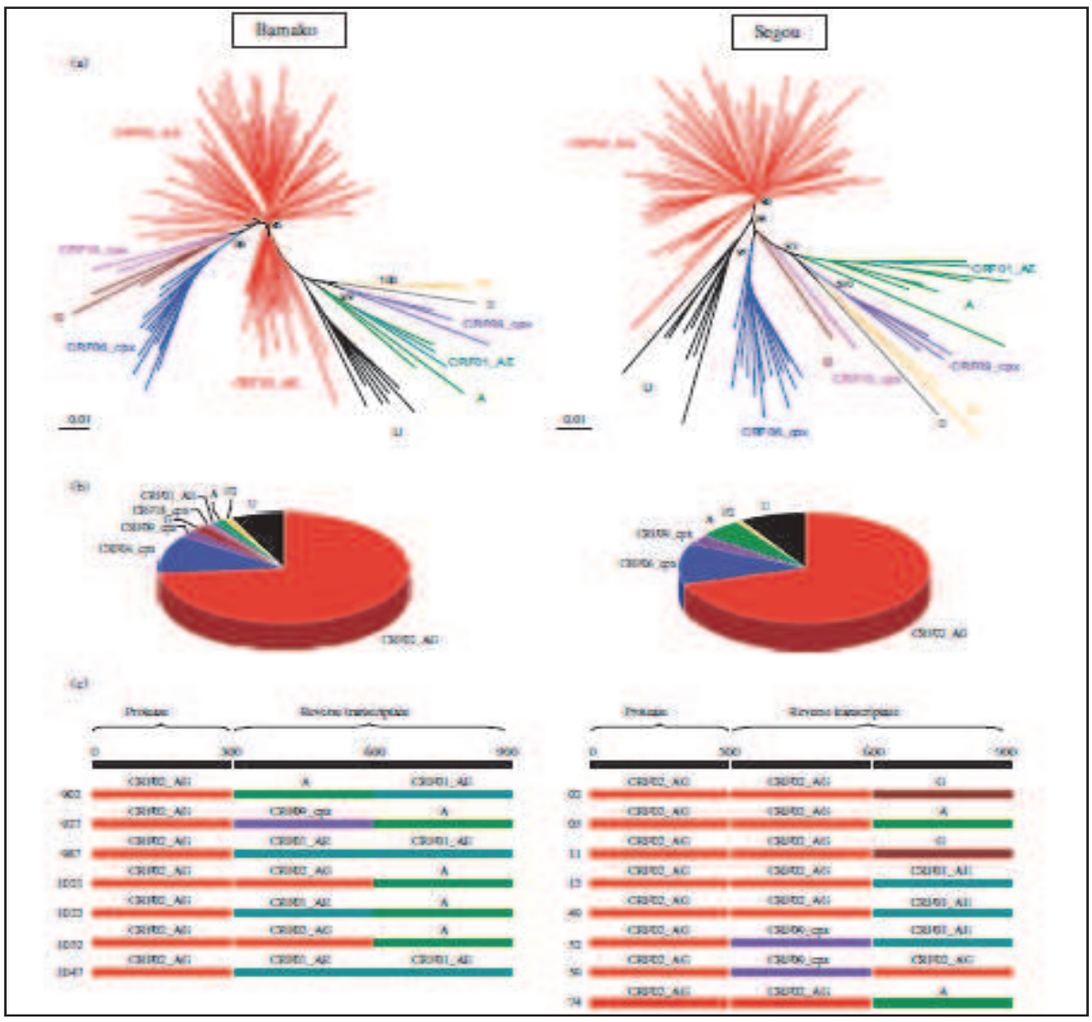


Fig. 2. Phylogenetic analysis from different subtypes in Mali. Results are presented for Bamako on the left and for Segou on the right. (a) Unrooted phylogenetic trees of pol nucleotides sequences. Sequences from references strains appear in bold. Each colour corresponds to a subtype or CRF. (b) Graphic representation of subtypes repartition. (c) pol gene mosaic viruses ('unknown U' viruses), with recombination points and subtypes involved. (Derache, 2008)

As seen from the phylogenetic data above (Fig. 1), Mali has a large genetic diversity of HIV-1 viral strains and the potential to generate new recombinants. While evaluating antiretroviral resistance of HIV strains in Mali a recent study conducted among 746 ARV treatment-naive HIV-1 patients showed that the majority carried the CRF02_AG subtype CRF06_cpx (Maiga, 2010). Indeed, many of the viruses sequenced in this study were either recombinant intersubtypes or had unique recombinant forms (URF). A large proportion 72%% of these were the recombinant CRF02_AG. It is therefore important to monitor the emergence and spread of new recombinants because the appearance of a particular polymorphism within a new recombinant could lead to resistance mutation profiles in individuals or a different response to antiretroviral therapy. For now, the CRF02_AG is believed to be the most prevalent (72%) in Mali and overall it appears to have similar characteristics to the subtype B.

The genetic variability of HIV viral strains involves genes encoding the viral enzymes, which are targets of therapeutic drugs. This variability occurs because of errors in viral reverse transcriptase. Knowledge of the genetic subtype as well as the inter-subtype recombinant nature of HIV-1 strains might be of crucial importance for the development of future HIV vaccine. Some substitutions of amino acids are found at high frequencies at positions involved in resistance to ARVs in subtype B. Thus, over 50% of non-B virus infecting in naive patients carry at least three PI resistance mutations, while it concerns only 8% of the virus subtype B (Holguin, 2002). To assess the impact of this polymorphism on resistance to ARVs, many phenotypic studies have been conducted on the gene for PR gene with many mutations of minor resistance in subtype non-B. Although many results conclude that patients infected with HIV-1 subtype non-B also respond well to treatment than patients infected by subtype B, some studies show a decreased sensitivity to certain subtypes IP. For example, the recombinant CRF02_AG, naturally bearing mutations K20I and M36I, replicates better in the presence of IP, thus reducing its sensitivity to these molecules, including NFV (Kinomoto, 2005). In addition, Perno et al demonstrated that the minor mutation M36I of PR gene, polymorphic in non-subtype B was predictive of virological failure after 24 weeks of antiretroviral therapy containing a PI, in fact, appearance of major mutations L90M during virologic failure was associated with the presence of the mutation M36I (Perno, 2004). A study in Uganda also showed that mutations associated with resistance to NVP was detected more frequently 6-8 weeks after delivery in women infected with subtype D than subtype A after taking a single dose of NVP in the context of PMTCT (Kiwanuka, 2008). The authors explain this result by a potential natural polymorphism of IT to push faster selection of resistance mutations to Nevirapine. A recent study conducted in Japan identified a new recombinant strain of HIV-2, CRF01_AB. Although no recombinant forms of HIV-2 have been found in Mali, there is a possibility that this new strain may soon be identified here, given that it was identified from samples obtained from Cote d'Ivoire (Ibe, 2010).

2.6 HIV drug resistance in Mali

The management of patients infected with HIV is complex and follows a long duration. It will therefore improve the quality of life of people living with HIV, if drug resistance is avoided. Several research studies on resistance mutations were performed in Mali. In 2007, Derache and colleagues evaluated the presence of resistance mutations in 98 naive patients receiving antiretroviral therapy, and showed the presence of K103N in two individuals. This mutation resulting in NNRTI resistance, render NVP or EFV inefficient (Derache, 2007). Similarly, another study estimated the presence of resistance mutations in 109 patients treated in Segou by Triomune ® (d4T +3 TC + NVP) in a median time of 8 months, and showed 11 cases of resistance to the presence of different mutations as follows: 2 cases of M184V alone, 1 case of Y181C alone, 8 cases including 5 associations Y181C + M184V, K103N + M184V + 2 and 1 association G190A + M184V K101E + G190A (Marcelin, 2007). These data demonstrates the need for the management of early failures to drug treatments and shows the importance of using other NRTIs in second-line treatments. Based on the 2007 version of an algorithm of interpretation by International AIDS Society (IAS) Derache and colleagues showed an overall prevalence for primary resistance of 11.5% (made up of 1.5% for NRTIs (K219Q), 9% to NNRTIs (Y181C, K101E, V90I, A98G and V106I and V108I) and 1% for PI (L33F and M46L)) (Derache, 2008). These identified mutations corresponded to the treatments used except for the mutations V90I, A98G and V106I which were associated with resistance to TMC 125 or Etravirine according to the IAS algorithm. No significant difference between 2005 and 2006 in

the prevalence of primary resistance of different classes of antiretroviral drugs has been observed. A similar study of treatment-naive patients recently showed a higher prevalence of primary resistance (9.9%) than was previously reported by Derache and colleagues (Haidara, 2010; Derache, 2008). So also have other studies reported late failures to drug treatment in Mali and in Burkina Faso with median treatment duration lasting 18 months (Sylla, 2008). Recently, two studies looked at resistance mutations among treatment-naïve patients in Mali. In the first study, 10% of patients failing second-line drug treatments were found to have failed therapy to all available drug molecules used in the country (Maiga, 2010). In the same study, resistance associated to ETR was found in ARV-naïve patients with HIV-1 subtype B. Previously, the genetic barriers to integrase inhibitors for HIV-1 subtype B had been compared to those of CRF02_AG and although they both have similar barriers, the CRF02_AG carried a higher genetic barrier at positions 140 and 151 of the integrase (Maiga, 2009). Thus, the finding in which ETR was implicated is important because it will facilitate the establishment of second and third line ARV treatments in a developing country such as Mali (Maiga, 2010). In the second study, of 57 HIV-2 treatment-naïve patients, 3 of 36 had a PR and RT-resistance mutation, implying that either resistant virus to these class strategy are circulating in Mali or the patients were taking ART without medical supervision. Of the remaining 21 patients, 1 had resistance mutations to both RT and PR, while a second had resistance to RT only. The presence of these mutations in both of these treatment-naïve patients indicates inadequate compliance to treatment (Oumar, 2010).

Although there is the risk that resistant viruses are spread throughout the country, and thereby pose an additional public health challenge, currently there is not enough data at the national level on the transmission of resistant virus. Despite this, the data shown from the studies mentioned above indicate the magnitude of the problem which may limit therapeutic choices in a resource-limited country such as Mali. And because, resistance is a major concern for long-term treatment in this place, it is necessary to improve adherence to treatment as well as routine monitoring to avoid an escalation of the evolution of primary resistance. One approach to resolving this is to broaden genotypic testing for treatment failures, and have a wider range of antiretroviral drug regimen to cover cases involving resistant strains. Although individual classes of antiretroviral are low, overall primary resistance in Mali is high. Exceptions are the NNRTIs which are relatively high (9%) probably due to their frequent use. In the past at least, a single-dose of NVP was used for the prevention of mother to child transmission and needs monitoring.

3. Conclusions/recommendations

Considerable efforts have been made towards HIV prevention and treatment in Mali. Lessons learnt from some epidemiological data showed that the efforts must be sustained in order to make significant changes to the behavior of young adults regarding HIV infection in Mali. As shown the prevalence of HIV alone is variable between social groups. Surprisingly, the prevalence among those co-infected with HIV and HBV was so high that this particular group must be targeted for further education and counseling. Despite this, it must be remembered that the biggest challenge is the rising numbers in circulating recombinant forms of HIV due to the occurrence of several mutations resistant to antiretroviral drugs. Therefore in Mali, there is an urgent need to increase access to antiretroviral drugs. In addition, newer approaches must be developed to improve compliance as well as follow up monitoring of viral load levels of the patients. Also, it will

be more useful if knowledge about HIV and the level and frequency of risk behaviors related to the transmission of HIV is stepped up as part of a national educational campaign, with the hope to change unsafe behaviors towards a better one.

4. Acknowledgements

We are grateful to the Malian Ministry of Health, Malian National HIV program and their partners particularly the ESTHER group, for giving us access to data on different national surveys, and to the University of Bamako for their support of this work. Funding was obtained from DCR/NIAID/NIH for this chapter.

5. References

Auerbach DM, Darrow WM, Jaffe HW,& Curran JW. 1984. Cluster of cases of the acquired immune Deficiency syndrome: patients linked by sexual contact. *Am J Med* 76: 487-492

Asamoah-Odei E, Garcia-Callga JM, & Boerma T. 2004. HIV prevalence and trends in sub-Sahara Africa: no decline and large subregional differences. *Lancet* 364: 35-40

Ballo MB, Traore SM, Niambele I, Ba S, Ayad M,& N'diaye S, 2001. Troisième Enquête Démographique et de Santé du Mali 2001 (EDSM-IV), *CPS/MS*, 332 pages.

Brun-Vezinet F , Katlama C , Roulot D, Lenoble L , Alizon M , Madjar JJ, Rey MA , Girard PM , Yeni P, Clavel F, Gadelle S , & Harzic M. 1987. "Lymphadenopathy-associated virus type 2 in AIDS and AIDS-related complex. Clinical and virological features in four patients." *Lancet* 1(8525): 128-32 Casado G,Thomson MM, Delgado E, Sierra M, Vazquez-De Parga E, Perez-Alvarez L, Ocampo A,& Najera R. 2003. Near full-length genome characterization of an HIV type 1 CRF05_DF virus from Spain. *AIDS Res Hum Retroviruses* 19:719-25.

Chamberland ME, Castro KG, Haverkos HW, Miller BI, Thomas PA, Reiss R, Walker J, Spira TJ, Jaffe HW,& Curran JW.1984.Acquired immunodeficiency syndrome in the United States: an analysis of cases outside high-incidence groups. *Ann Intern Med.* Nov;101(5):617-23.

Clavel F. (1987). "HIV-2, the West African AIDS virus." *AIDS* 1(3): 135-40.

Clavel F, Mansinho K, Chamaret S, Guetard D, Favier V, Nina J, Santos-Ferreira MO, Champalimaud JL, & Montagnier L. 1987. Human immunodeficiency virus type 2 infection associated with AIDS in West Africa. *N Engl J Med* 316:1180-5.

Derache A, Maiga AI, Traore O, Akonde A, Cisse M, Jarrousse B, Koita V, Diarra B, Carcelain G, Barin F, Pizzocolo C, Pizarro L, Katlama C, Calvez V,& Marcelin AG. 2008. Evolution of genetic diversity and drug resistance mutations in HIV-1 among untreated patients from Mali between 2005 and 2006. *J Antimicrob Chemother* 62:456-63.

Derache A, Traore O, Koita V, Sylla A, Tubiana R, Simon A, Canestri A, Carcelain G, Katlama C, Calvez V, Cisse M,& Marcelin AG. 2007. Genetic diversity and drug resistance mutations in HIV type 1 from untreated patients in Bamako, Mali. *Antivir Ther* 12:123-9.

Diarra A, Kouriba B, Baby M, Murphy E, Lefrere JJ, 2009. HIV, HCV, HBV and syphilis rate of positive donations among blood donations in Mali: lower rates among volunteer blood donors. *Transfus Clin Biol.*16(5-6):444-7.

Haidara A, Chamberland A, Sylla M, Aboubacrine SA, Cissé M, Traore HA, Maiga MY, Tounkara A, Nguyen VK,& Tremblay C; Appuyer le Traitement Anti Rétroviral en Afrique de l'Ouest (ATARAO) Group 1. 2010. High level of primary drug resistance in Mali. *HIV Med.* 1;11(6):404-11.

Holguin, A, Alvarez A, & Soriano V. 2002. High prevalence of HIV-1 subtype G and natural polymorphisms at the protease gene among HIV-infected immigrants in Madrid. *AIDS* 16:1163-70.

Korber A, Dissemond J, Hillen U, Goos M,& Esser S. 2003. [HIV-positive patient with multiple ulcers. Lues maligna]. *Hautarzt* 54:1098-102.

Korber B, Muldoon M, Theiler J, Gao F, Gupta R, Lapedes A, Hahn BH, Wolinsky S, & Bhattacharya T. 2000. Timing the ancestor of the HIV-1 pandemic strains. *Science* 288:1789-1796.

Kinomoto M, Appiah-Opong R, Brandful JA, Yokoyama M, Nii-Trebi N, Ugly-Kwame E, Sato H, Ofori-Adjei D, Kurata T,Barre-Sinoussi F, Sata T, & Tokunaga K. 2005. HIV-1 proteases from drug-naive West African patients are differentially less susceptible to protease inhibitors. *Clin Infect Dis* 41:243-51.

Kiwanuka N, Laeyendecker O, Robb M, Kigozi G, Arroyo M, McCutchan F, Eller LA, Eller M, Makumbi F, Birx D, Wabwire-Mangen F, Serwadda D, Sewankambo NK, Quinn TC, Wawer M,& Gray R. 2008. Effect of human immunodeficiency virus Type 1 (HIV-1) subtype on disease progression in persons from Rakai, Uganda, with incident HIV-1 infection. *J Infect Dis* 197:707-13.

Laukkanen T, Carr JK, Janssens W, Liitsola K, Gotte D, McCutchan FE, Op de Coul E, Cornelissen M, Heyndrickx L, van der Groen G, & Salminen MO. 2000. Virtually full-length subtype F and F/D recombinant HIV-1 from Africa and South America. *Virology* 269:95-104.

Maiga A, Fofana DF, AIT-ARKHOUB Z, Cissé, M, Diallo F, Haidara M, Traoré HA, Coulibaly H, Akonde A, Pizarro L, Brucker G, Murphy R, Katlama C, Tounkara A, Marcelin AG,& Calvez V. 2010. "Echec Virologique aux traitements Antirétroviraux de seconde ligne et Profil des Mutations de Résistance chez des Patients infectés par le VIH-1 à Bamako au Mali." *5ème Conférence francophone Casablanca Maroc* 28 - 31 Mars.résumé N° 333

Maiga AI, Descamps D, Morand-Joubert L, Malet I, Derache A, Cisse M, Koita V, Akonde A, Diarra B, Wirden M, Tounkara A, Verlinden Y, Katlama C, Costagliola D, Masquelier B, Calvez V,& Marcelin AG. 2010. Resistance-associated mutations to etravirine (TMC-125) in antiretroviral-naive patients infected with non-B HIV-1 subtypes. *Antimicrob Agents Chemother* 54:728-33

Maïga AI, Malet I, Soulie C, Derache A, Koita V, Amellal B, Tchertanov L, Delelis O, Morand-Joubert L, Mouscadet JF, Murphy R, Cissé M, Katlama C, Calvez V,& Marcelin AG. 2009. Genetic barriers for integrase inhibitor drug resistance in HIV type-1 B and CRF02_AG subtypes. *Antivir Ther.*;14(1):123-9.

Maïga I, Le Faou A, Muller CP, & Venard V.2005. Unexpected high prevalence of hepatitis B and HIV infections in Malian medical students. *Eur J Clin Microbiol Infect Dis.* Jul;24(7):501-2.

Marcelin AG, Jarrousse B, Derache A, Ba M, Dakouo ML, Doumbia A, Haidara I, Maiga A, Carcelain G, Peytavin G, Katlama C,& Calvez V. 2007. HIV drug resistance after the use of generic fixed-dose combination stavudine/lamivudine/nevirapine as standard first-line regimen. *AIDS* 21:2341-3.

McCutchan F E, Sankale JL., M'Boup S, Kim B, Tovanabutra S, Hamel DJ, Brodine SK, Kanki PJ,& Birx DL. 2004. HIV type 1 circulating recombinant form CRF09_cpx from west Africa combines subtypes A, F, G, and may share ancestors with CRF02_AG and Z321. *AIDS Res Hum Retroviruses* 20:819-26.

Oumar AA, Dao S, Lambert C, Traoré S, Katile D, Sidibé Y, Tulkens PM, Goubau P, & Ruelle J.2010. Traitement du VIH-2 au Mali et Profil de résistance aux antirétroviraux. 5ème *Conférence Francophone VIH/Sida, Casablanca* Maroc du 28-31 Mars 2010. Abstract N°170/33A

Peeters M, & Delaporte, E. 1999. Genetic diversity of HIV infection worldwide and its consequences. *Med Trop* (Mars). 1999;59(4 Pt 2):449-55.

Perno C F, Cozzi-Lepri A, Forbici F, Bertoli A, Violin M, Stella Mura M, Cadeo G, Orani A, Chirianni A, De Stefano C, Balotta C,& d'Arminio Monforte A. 2004. Minor mutations in HIV protease at baseline and appearance of primary mutation 90M in patients for whom their first protease-inhibitor antiretroviral regimens failed. *J Infect Dis* 189:1983-7.

Pichard E, Guindo A, GrossetteG, Fofana Y, Maiga Y I, Koumare B, Traore S, Maiga M, Brun-Vezinet F, & Rosenheim M, 1988. L'infection par le virus de l'Immunodéficience humaine (VIH) au Mali. *Med Trop* 48 (4) ; 345-349

Samake S, Traore SM, Ba S, Dembele E, Diop M, Mariko S,& Libite PR. 2006. Quatrième Enquête Démographique et de Santé du Mali 2006 (EDSMIV), CPS/MS, 410 pages

Selik RM, Harverkos HH, Curran JW. 1978. Acquired immune deficiency syndrome (AIDS) trends in the United States, 1978-1982. *Am J Med*. 76: 493-500

Sidibe T, Sangho H, Traore MS, Cissé MB, Diallo B, Keîta MM,& Gendrel D. 2006. Knowledge, attitudes, and practices of adolescents in an urban school environment in Bamako, Mali, around family planning, sexually transmitted infections, and AIDS]. *Mali Med.*;21(1):39-42.

Sylla M, Chamberland A, Boileau C, Traoré HA, Ag-Aboubacrine S, Cissé M, Koala S, Drabo J, Diallo I, Niamba P, Tremblay-Sher D, Machouf N, Rashed S, Nickle DC, Nguyen VK, & Tremblay CL; ATARAO Group. 2008. Characterization of drug resistance in antiretroviral-treated patients infected with HIV-1 CRF02_AG and AGK subtypes in Mali and Burkina Faso. *Antivir Ther*. ;13(1):141-8.

TCHOUZOU Tabeth Hilaire, 2008. Evaluation des connaissances, comportements et attitudes a risk de l'infection VIH /SIDA dans la population carcérale de la maison d'arrêt de Bamako.*These de Medecine, Universite de Bamako, Mali*

Thomson MM, Casado G, Posada D, Sierra M,& Najera R. 2005. Identification of a novel HIV-1 complex circulating recombinant form (CRF18_cpx) of Central African origin in Cuba. *AIDS* 19:1155-63.

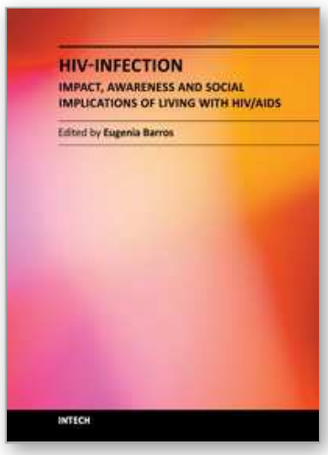
UNIAID/WHO. AIDS epidemic update, December, 2005. UNIAID/WHO; Genevor, Switszerland

UNAIDS/WHO. AIDS epidemic update. December 2010. www.unaids.org

White HL, Kristensen S, Coulibaly DM, Sarro YS, Chamot E,& Tounkara A. 2009. Prevalence and predictors of HIV infection amongst Malian students. *AIDS Care*. Jun;21(6):701-7.

WHO, UNAIDS, UNICEF. Towards universal access. Scaling up priority HIV/AIDS interventions in the health sector. Progress report 2009. Geneva:WHO press; 2009.pp.1-162.

World Health Organisation. Rapid advice. Antiretroviral therapy for HIV infection in adults and adolescents. Geneva:WHO press;2009.pp.1-25. www.who.int/hiv/pub/arv/rapid_advice_art.pdf



HIV-infection - Impact, Awareness and Social Implications of living with HIV/AIDS

Edited by Dr. Eugenia Barros

ISBN 978-953-307-343-9
Hard cover, 336 pages
Publisher InTech
Published online 26, October, 2011
Published in print edition October, 2011

The past few decades have seen the escalation of HIV-infections and the 'frantic' search for new drugs to treat the millions of people that live with HIV-AIDS. However because HIV-AIDS cannot be cured, but only controlled with drugs, and the Antiretroviral (ARV) treatment itself results in some undesirable conditions, it is important to generate wider awareness of the plight of people living with this condition. This book attempts to provide information of the initiatives that have been used, successfully or unsuccessfully, to both prevent and combat this 'pandemic' taking into consideration the social, economic, cultural and educational aspects that involve individuals, communities and the countries affected.

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen