Twenty Years of Human Immunodeficiency Virus Infection in Croatia – An Epidemic that is Still in an Early Stage

Josip Begovac¹, Šime Zekan¹ and Dunja Skoko-Poljak²

¹ University Hospital for Infectious Diseases, Zagreb, Croatia
² Department of Professional Medical Affairs, Ministry of Health and Social Welfare, Zagreb, Croatia

ABSTRACT

Croatia has a low-level HIV epidemic; 553 persons were diagnosed with HIV infection in the period 1985–2005. The principal mode of transmission was sex between men (40% of cases) and heterosexual contact (40%). Only about 10% of cases were injecting drug users. Testing data also suggest a low prevalence of HIV infection in Croatia, even in vulnerable groups. Behavioral data indicate risky sexual behaviors, with the clear need for interventions. National policy towards HIV/AIDS is operated through the National Committee on HIV/AIDS, a multisectorial advisory body to the Government of Croatia. Croatia applied to the Global Fund to fight AIDS, tuberculosis and malaria in 2002 which resulted in a 4.9 million USD grant for scaling up prevention interventions. Croatia has a centralized system of treatment and care which is provided at the University Hospital for Infectious Diseases in Zagreb. Highly active antiretroviral treatment is provided free of charge from April 1998.

Key words: HIV, AIDS, epidemic, Croatia

Introduction

The first serologically confirmed cases of human immunodeficiency virus (HIV) infection in Croatia were identified in October 1985. The first two patients with the acquired immunodeficiency syndrome (AIDS) were hospitalized at the University Hospital for Infectious Diseases (UHID) in 1986. Both patients were returnees from Western European countries where HIV infection was already diagnosed. Both were males and acquired HIV through sex with males. Both patients died the same year, the first suffered from AIDS-encephalopathy and the second was admitted to the hospital with respiratory failure caused by pneumonia. The first publicly known patient with HIV infection was a hemophiliac from a rural town (Podravska Slatina) in Slavonia. The beginning of the HIV/AIDS in Croatia was met with fear, concerns about the extend of the epidemic, and accompanied by stigma and social exclusion of those infected with HIV.

Demographics

Croatia is a small, upper-middle income country with a population of 4.4 million. It is a Middle or Southeastern European country with 1 778 km of coastline on the Adriatic Sea, extending landward between Slovenia, Hungary, Serbia, Bosnia and Herzegovina and Montenegro. Croatia’s birth rate has decreased dramatically over the past 15 years and the annual number of births is currently 40 307 per year (2005)¹. Infant mortality is 4.4 ‰¹. Net primary school enrolment/attendance is high (89%) (1996–2004)², total adult literacy rate is 98% (2000–2004)² and life expectancy at birth is 72 years for men and 79 for women¹. In the past two decades Croatia has been affected by many social and economic changes including the 1991–1995 war for independence. This had also an impact in terms of migration and life loses. It has been estimated that Croatia lost about 10% of its population during the period 1991–1995. It has also been estimated that in the period 1994–1998, 224 175 persons immigrated into Croatia and 61 726 emigrated from Croatia¹. Not only the war but also the change from a communist economic system towards a market driven economy has made great economic and social impact. The current situation is now also characterized by a relatively high unemployment rate 17.9% (2005)³, a relatively high cost of...
living and accumulation of wealth to few individuals and their families. The economy is greatly tourism based. The gross domestic product per capita is estimated to be 8674.4 USD in 2005. However, despite the 1991-1995 war events and other economical difficulties typical for a transition to a market economy no large-scale increase in HIV/AIDS cases has been observed.

Status of the Epidemic

In Croatia, cases of HIV infection and AIDS are notifiable on a named basis. Based on figures from HIV/AIDS Register at the Croatian National Institute of Public Health (IPH) a total of 553 patients with HIV infection have been diagnosed in the period 1985–2005. Of those 239 had AIDS and 127 died. There was an 8 to 13% yearly increase of the total number of HIV/AIDS cases in the period 2001–2005 (Figure 1). The incidence is also slowly increasing it was between 6 to 14 cases per million in the period 2001–2005 (Figure 2). Hence, the epidemic is still in its early initial increasing stage. The number of deaths is decreasing after the introduction of highly antiretroviral treatment (HAART) there have been 3 to 6 deaths per year in the period 2001–2005. In summary, despite the slow increase of HIV cases over time, Croatia is a country with a low level HIV epidemic.

The principal modes of HIV transmission in Croatia are sex between men (40%) and heterosexual contact (40%). Eighty-percent of all HIV infections are in males and 65% of all cases are between 25 and 44 years old at the time of HIV diagnosis. In the beginning almost all patients had verified or presumed history of exposure to HIV outside Croatia, regardless of the mode of transmission. Currently, new cases of HIV infection reported among men having sex with men are largely domestic, whereas the majority of cases acquiring HIV through heterosexual contact are still from outside the country. Although drug use is on the rise in Croatia, only about 10% of all HIV cases acquired the infection through injecting drugs. Data collected from injecting drug users in treatment programs and needle exchange programs have also indicated a low prevalence of HIV infection (Figure 3). Even prior to the HIV epidemic, the Centre for Hemophilia in Zagreb has insisted on giving locally derived cryoprecipitate (from known voluntary blood donations) whenever possible, rather than offering imported factors. This resulted in a low prevalence of HIV infection among hemophiliacs (only 13 cases). There have been recently two cases of post-transfusion HIV infection in Croatia from a single donor in the window period. There have been only nine cases of mother-to-child transmission. The last known cases of mother to child HIV transmission occurred in 2000.

Testing Data

HIV testing for blood and blood products has been mandatory in Croatia since 1987. There is a well-organized network of blood transfusion centers in Croatia and all of them perform HIV screening on each blood sample.

Prior to the Global Fund project there were only two voluntary counseling and testing (VCT) sites in Croatia. These testing sites were at the University Hospital for Infectious Diseases (UHID) in Zagreb and at the Clinical Center Rijeka. HIV testing, albeit with limited counseling, has also been performed at Transfusion centers in Zagreb. HIV testing for blood and blood products has been mandatory in Croatia since 1987. There is a well-organized network of blood transfusion centers in Croatia and all of them perform HIV screening on each blood sample.

Prior to the Global Fund project there were only two voluntary counseling and testing (VCT) sites in Croatia. These testing sites were at the University Hospital for Infectious Diseases (UHID) in Zagreb and at the Clinical Center Rijeka. HIV testing, albeit with limited counseling, has also been performed at Transfusion centers throughout Croatia. The Global Fund project enabled us to open altogether 10 VCT sites during 2004 and 2005. Positive HIV screening tests are sent to the Reference Laboratory at UHID in Zagreb where confirmatory testing is performed. Anonymous testing was not widely available before the Global Fund project. However, all

Fig. 1. Increase in reported HIV cases in Croatia, 1995–2005.

Fig. 2. Newly diagnosed HIV infections per million total population, by year in Croatia, 1995–2005. The population of Croatia used in this calculation was 4.5 million.

Fig. 3. Percentage of HIV positive tests in injecting drug users (IDU) and in voluntary testing and counseling centers (VCT) plus clinical settings in the period from 2001 to 2005. Duplicates are not sorted out.
citizens of Croatia are entitled to Health Care Insurance and HIV testing was free of charge if proof of insurance was presented. Testing is also performed on clinical grounds in different inpatient and outpatient setting. In those cases the tests are usually performed at transfusion units. IPH collects annual data on the number of HIV tests performed in every setting. The number of tests performed and the number of positive results are presented on Figure 3. Interestingly, it seems that the annual number of tests performed in Croatia did not increase after opening of VCT Centers in 2004 and 2005 (Figure 3). However, the number of newly diagnosed HIV infections did increase in 2005. Preliminary data from 2006 do not confirm the increase of newly diagnosed HIV infections seen in 2005. The data on HIV infection among injecting drug users come from testing conducted at needle exchange programs and from patients included in the methadone program or other treatment settings. The data on the number of positive tests among blood donation also suggest a low incidence of HIV in Croatia. Between 2001 and 2005 there have been 0 to 2.8 positive tests per 100 000 donations. Formal HIV seroprevalence studies using appropriate sampling methods have thus far not been conducted among vulnerable groups. An anonymous unlinked serosurvey was conducted in 2005 on left–over blood samples from different hospitals in Croatia from three major cities (Zagreb, Split, Rijeka). Out of 3357 individuals 3 were positive (0.089%, 95% confidence interval by the Blyth-Still-Casella method was 0.024% to 0.250%). In conclusion, the testing data is consistent with a low level epidemic.

Behavioral Data

There are several target populations for whom behavior data is available. Unfortunately, the majority of surveys have not been published in internationally peer-reviewed journals and the majority of studies targeted school children or students in major Croatian cities. Most studies reported good knowledge about HIV/AIDS. Condom use at last sexual intercourse varied from 43% to 73% in more recent reports. The only national-based survey with a probabilistic sample has been conducted in 2005. It surveyed 1093 participants aged 18 to 24 years. The data on the number of positive tests among blood donation also suggest a low incidence of HIV in Croatia. Between 2001 and 2005 there have been 0 to 2.8 positive tests per 100 000 donations. Formal HIV seroprevalence studies using appropriate sampling methods have thus far not been conducted among vulnerable groups. An anonymous unlinked serosurvey was conducted in 2005 on left–over blood samples from different hospitals in Croatia from three major cities (Zagreb, Split, Rijeka). Out of 3357 individuals 3 were positive (0.089%, 95% confidence interval by the Blyth-Still-Casella method was 0.024% to 0.250%). In conclusion, the testing data is consistent with a low level epidemic.

There is generally a lack of data on risk behavior in vulnerable populations. In a rapid assessment and response on HIV/AIDS in mainly young injecting drug users lifetime sharing of needles and equipment varied between Croatian cities from 40 to 70%. There was fewer needle sharing in cities with needle exchange programs. Furthermore, behaviors that might favor rapid spread of HIV such as shooting galleries were not observed. Risky sexual behavior was prevalent in this study population, only 9.3% of girls and 13% of boys were using condoms regularly. According to the data from the National Report on Illicit Drug Use published by the Croatian Institute of Public Health 6642 persons were treated for substance abuse in different health care setting in Croatia (data from non-governmental organizations and from treatment communities are not included) in 2005. Opiate use was recorded in 4866 (73%) persons and lifetime needle sharing in 71.3%. There was a trend of lower needle-sharing in the last one month among persons enrolled into treatment in more recent years between 2002 and 2005 (38.6% 33.1% 28.6% and 23.0%, respectively). The only study on sexual behavior among men who have sex with men (MSM) was conducted by the Croatian Institute for Public Health and ISKORAK a non-governmental organization for gay rights in 2006. The results of the study were recently presented in media. Altogether 1127 gay men were interviewed. The interview took place in bars, saunas and over the web. When asked about the number of partners with whom they engaged in anal intercourse during the last 12 months 15% reported no sexual partner, 27% had one, 12% had two, 28% had between 3 and 10 and 18% reported more than 10 partners. 18% of gay men never used a condom when engaging in anal intercourse, and consistent condom use was reported in 47% of gay men. 57% used a condom at the last anal intercourse. 53% of gay men reported never having an HIV test.

Data on migrant workers are also only recently emerging. In the Global Fund Project sponsored research project on HIV/AIDS related knowledge, attitudes, and patterns of sexual behavior in Croatian migrant workers of 242 predominantly seamen only 61% used a condom at last intercourse with a casual partner. Unfortunately despite the fact that the first cases of HIV/AIDS were diagnosed in labor migrants, there is little data on the sexual behavior of Croatian labor migrants and returnees from Western European countries. It is assumed that labor migrants, particularly if their spouses do not accompany them, change their sexual behaviors in the host country and perhaps engage into sex for money. However, as labor migrants seem to be better targeted in the host country the number of HIV infected returnees is presently relatively small. Unfortunately, there have been cases of suboptimal treatment and expulsions of HIV infected Croats from Western European countries.

There is little behavioral and testing data from sex workers in Croatia. In 1993, 100 women from three major cities were voluntarily tested and all tests were negative for HIV infection.
In conclusion, behavioral data do indicate risky sexual behaviors. Particularly worrisome are the data on MSM. Behavioral and biomedical interventions are needed to prevent the wider spread of HIV, particularly in MSM.

Response to HIV/AIDS

Government and non-governmental organizations

Up to 1991 Croatia was one of the republics within the former Yugoslavia. In the beginning of the AIDS epidemic in Yugoslavia it was decided that HIV infected patients should be treated at 3 centers: Ljubljana, Zagreb and Belgrade. There were only two confirmatory HIV testing sites, one in Ljubljana and the other in Belgrade. However, a local Zagreb prevention committee was also established in 1987. An intensive education campaign was at that time introduced in Zagreb, focusing mainly on the youth. However, the campaign was not sustained over the years and was mostly dependent on individual efforts of schoolteachers and school children.

A Reference Center for HIV/AIDS was established at UHID in 1992. The main goals of the Reference Center are to perform confirmatory HIV testing, develop diagnostic and treatment guidelines for HIV/AIDS and opportunistic infections and to treat HIV infected patients.

Soon after the proclamation of independence of Croatia, at the Ministry of Health of Croatia, an HIV/AIDS Prevention Committee was established in 1992. The Croatian Government has accepted the National HIV/AIDS Prevention Program in 1993. Its major task was to formulate a national policy towards HIV/AIDS. In the early years the National AIDS Committee had usually very limited funds for prevention activities (up to 20 000 USD per year). With this limited funds the Ministry of Health has on several occasions funded posters, videos, and TV ads on HIV/AIDS prevention. It supported the publishing of leaflets, a publication for people living with HIV/AIDS and for health care workers and a manual for adolescents on HIV/AIDS. It also supported a book on HIV/AIDS. The Ministry of Health also supported and funded the introduction of needle exchange program in Split in 1996/1997. Although formed within the Ministry of Health is the principle recipient of the 4.9 million grant of the GFATM.

In December 2001 the Committee initiated a process of revising and updating the National AIDS Strategy. After extensive consultations and input from many governmental and non-governmental organizations the revised National HIV/AIDS Plan was accepted by the Croatian government in 2005. The revised strategy aims to ensure that Croatia remains a low prevalence country. It emphasizes the need to strengthen interventions for vulnerable groups (IDU and MSM), ensure the continued full provision of HAART by the Croatian Health Insurance Institute, scale up prevention particularly among youth, diversify voluntary counseling and testing (VCT) services, strengthen advocacy for PLWHA and other highly stigmatized groups and introduce second-generation surveillance.

Treatment and care

Croatia has a centralized system of care and all HIV infected patients are treated at the HIV/AIDS center at UHID. There were relatively few patients in care up to 1995. Most patients were hospitalized with major opportunistic diseases and the median survival after an AIDS diagnosis was 18.8 months in the period 1985–1998. Although a range of opportunistic infections have been diagnosed, the two most frequent were tuberculosis...
and *Pneumocystis jiroveci* pneumonia (PCP). Very few patients received PCP prophylaxis or zidovudine therapy before 1992; out of 36 AIDS patients in care before 1992 only 2 patients used zidovudine and 3 PCP prophylaxis. Protease inhibitors became reimbursed by the Croatian National Health Insurance in April 1998; however, 12 patients already used them in 1997. Unfortunately, patients had to pay for the protease inhibitor before April 1998, which sometimes contributed to the interruption or suboptimal antiretroviral treatment. Survival following the first AIDS-defining illness markedly improved in the period 1997–2000 compared to the period 1986–1996 (adjusted Hazard Ratio for patients surviving more than 6 months: 0.11). The number of patients taking HAART increased over time (Figure 4) and presently (August 8th 2006) 277 patients are receiving it. The process of registration and approval of antiretrovirals has usually been slow. Currently (September 2006) the following antiretrovirals are on the Croatian National Insurance Drug List: zidovudine, lamivudine, zidovudine plus lamivudine, stavudine, didanosine, abacavir, nevirapine, efavirenz, indinavir, ritonavir, nelfinavir and lopinavir/ritonavir. All antiretrovirals on the Drug List are provided free of charge. Presently tenofovir and the newly developed fixed combinations of antiretrovirals (Truvada™ and Kivexa™) are not available in Croatia. Posamprenavir and atazanavir, and drugs used as salvage regimens such as enfuvirtide, tipranavir and darunavir are also not registered in Croatia in 2006. Of the 277 patients taking antiretrovirals the following combinations are more frequently used: zidovudine plus lamivudine plus efavirenz (62, 22.4%), zidovudine plus lamivudine plus lopinavir/ritonavir (40, 14%), zidovudine plus lamivudine plus nevirapine (31, 11.2%) and abacavir plus lamivudine plus efavirenz (31, 11.2%). The average monthly cost of antiretrovirals for one patient is approximately 800 USD. Through the support of the GFATM project an Outpatient Center for HIV/AIDS has been opened in June 2005 at UHID. Psychosocial support is an integral part of this Outpatient Center. HIV infected patients need no referral from primary care physicians (usually required for other diseases) to enter care at UHID. Antiretrovirals are also given to patients at UHID from the hospital pharmacy. There is a close collaboration of VCT centers and other hospitals with UHID. A small renal dialysis unit for HIV infected patients has been opened at UHID in 2005.

**International**

There was little support from international agencies in the period 1991–1995. After that, many international organizations have supported some prevention activities. However, the support was usually limited to small-scale projects. UNICEF has supported the Department of Reproductive Health at the Children’s Hospital in Zagreb, including HIV/AIDS prevention activities for youth. Open Society Institute (OSI) – Croatia has conducted seminars on healthy lifestyles and published posters and leaflets on World AIDS Day on several occasions. United Nations Drug Control Program (UNDCP) developed a report on illicit drug abuse in Croatia in 1999. UNICEF in conjunction with the International Organization for Migration (IOM) published an overview of HIV/AIDS in South Eastern Europe in 2002. The role of international agencies became more visible after formation of a UN theme group from representatives of different organizations (UNDP, WHO, UNHCR, World Bank, UNICEF, IOM, IFRC etc.) in November 2000. The Chair of the UN Theme Group on HIV/AIDS is included in the CCM.

IOM has recently conducted several projects on mobile populations for the whole region. UNICEF has also recently supported an analysis of Croatian legislation as related to HIV.

There were few small-scale collaborations addressing research and training of health care professionals. A training of Croatian physicians on HIV/AIDS took place at the National Institute for Infectious Diseases Lazzaro Spallanzani in Rome in 1998. A collaboration between the University of California San Francisco, School of Public Health – Andrija Stampar and UHID resulted in seminars on Designing Clinical Research in HIV/AIDS conducted in Croatia from 2003. Few pilot studies have been conducted as a result of this cooperation. An HIV/AIDS Training course for infectious disease specialists from the Western Balkans was held in Zagreb in October 2004, organized by Project Hope. WHO has recently chosen the Andrija Stampar School of Public Health in Zagreb as a place for Training in the 2nd Generation Surveillance of HIV/AIDS for the Countries of Central and Eastern Europe and Central Asia.

However, the most prominent impact on scaling-up prevention of HIV/AIDS in Croatia was the GFATM donation. The 3-year GFATM project started in November 2003. The focus of the project included almost all prevention activities planned by the National Prevention Plan.

![Graph](image-url)
Future Challenges

There are many factors that might contribute to the spread of HIV in Croatia: a relatively large number of IDUs, risky sexual behaviors among MSM, mobile populations and a tourism based economy. Hence the main challenge is to keep the incidence of HIV as low as possible. There are however several issues that need to be addressed on a policy level. There is at present no consensus on the type of sexual education in elementary and high school level. The controversial concept of ABC (abstinence, be faithful and condom) has been suggested but even without the C (condom) component. It should be understood that there is no scientific evidence that abstinence only programs work. Although initiatives for better education on HIV prevention of MSM are in progress particularly by NGOs, prevention of HIV among MSM is hampered by homophobia and stigmatization. Commercial sex work is illegal in Croatia. Hence sex workers who are not Croatian citizens, and thus are not entitled to the universal Croatian Health Insurance Scheme, have limited access to health care services. Although Croatia appears to be a transit country for human trafficking, there have been recent reports of women forced into sex work in Croatia. Discriminatory legislation, particularly in the workplace (example: HIV infected persons can not be sailors) does exist and needs to be changed. Unfortunately HIV infected patients are still stigmatized in the health care sector and in the society as a whole.

Croatia has thus far been successful in curtailing the epidemic in IDUs. This success might be partially explained by the early introduction of needle exchange programs through NGOs. The first needle exchange program has opened in Split in late 1996. Needle sharing practices that favor the spread of HIV, such as shooting galleries, have as yet not been observed in Croatia. The methadone program is presently widely available through primary care physicians. However, since Croatia has one of the higher rates of injection drug use in Europe we must be vigilant about preventing the epidemic in this population. The coverage of IDUs with harm-reduction services is presently unknown. Based on an estimation of about 10,000 heroin injectors the coverage might be estimated to be around 50–60%.

One of the major challenges is sustaining the prevention efforts mobilized by the GFATM donation. There are concerns that some activities might not get enough funding after the GFATM projects stops. HIV/AIDS in Croatia is presently not a priority in political discussions and political leaders rarely speak about HIV/AIDS. So, it is up to the professionals in different fields of expertise to pressure the national, regional and local governments for funding for HIV prevention and care.

In conclusion, no large scale HIV epidemic has developed during the first 20 years of HIV/AIDS in Croatia. Croatia has a low-level epidemic, which is still in an initial stage. Despite the many conditions that might favor the spread of HIV infection, as outlined above, we agree that there is only a moderate risk of a larger HIV infection outbreak in Croatia. This is so because Croatia has also a long history of prevention efforts and even with limited resources we have been able to allocate funds to activities that might have the greatest potential for averting a large-scale epidemic such as, for example, harm-reduction services.

Data Collection Strategy:

We searched the following web pages for data on Croatia and HIV/AIDS:

URL: http://www.dzs.hr;
URL: http://www.unicef.org/infobycountry/croatia_statistics.html;
URL: http://www.plivazdravlje.hr/?section=arhiva&cat=t&acat=t&show=1&id=2772;
URL: http://www.hzjz.hr;
URL: http://www.gay.hr/portal/opsirno-3678.php;
URL: www.mzss.hr;

We also reviewed all international documents concerning HIV/AIDS in Croatia (see references). The data on HIV/AIDS expenditures in Croatia came from the yearly report of the National HIV/AIDS Committee. Finally we also searched the PubMed database for publications on HIV/AIDS in Croatia using key words (Croatia, HIV, AIDS) and names of Croatian authors.
Acknowledgments

The authors of this paper presented their professional and personal views, not the views of institutions they work in or committees they are members. We also thank dr. Branko Kolaric for providing data from the Croatian HIV/AIDS register.

REFERENCES


J. Begovac
University Hospital for Infectious Diseases -Dr Fran Mihaljević, Mirogojska 8, 10000 Zagreb, Croatia
e-mail: jbegovac@bfm.hr

DVADESET GODINA HIV INFEKCIJE U HRVATSKOJ: EPIDEMIJA KOJA JE JOŠ UVIJEK U POČETNOM STADIJU

SAŽETAK