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Nationwide HIV prevalence survey in general population in Niger

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Summary A national population-based survey was carried out in Niger in 2002 to assess HIV prevalence in the population aged 15–49 years. A two-stage cluster sampling was used and the blood specimens were collected on filter paper and tested according to an algorithm involving up to three diagnostic tests whenever appropriate. Testing was unlinked and anonymous. The refusal rate was 1.1% and 6056 blood samples were available for analysis. The adjusted prevalence of HIV was 0.87% (95% CI, 0.5–1.3%) and the 95% CI of the estimated number of infected individuals was 22 864–59 640. HIV-1 and HIV-2 represented, respectively, 95.6% and 2.9% of infections while dual infections represented 1.5%. HIV positivity rate was 1.0% in women and 0.7% in men. It was significantly higher among urban populations than among rural ones (respectively, 2.1% and 0.6%, $P < 10^{-6}$). Using logistic regression, the variables significantly related to the risk of being tested positive for HIV were urban housing, increasing age and being either widowed or divorced. The estimate from the national survey was lower than the prevalence assessed from antenatal clinic data (2.8% in 2001). In the future, the representativeness of sentinel sites should be improved by increasing the representation of rural areas accounting for more than 80% of the population. Compared with other sub-Saharan countries, the HIV prevalence in Niger is still moderate. This situation represents a strong argument for enhancing prevention programmes and makes realistic the projects promoting an access to potent antiretroviral therapies for the majority.

keywords HIV, prevalence, population-based survey, randomized sample, dried blood spots, adults, Niger

Introduction

Niger is a sub-Saharan country of 1 267 000 km^2. The population was about 10.6 m in 2001, of whom 4.6 m were aged 15–49 years. Although scattered, the population is mainly concentrated in the southern part of the territory and 84% live in rural areas. The capital and main town, Niamey, had a population of 0.6 m and other large cities are few. The country is located on a commercial route connecting coastal countries of the Guinea Gulf and Algeria and Libya in the north. Most of the inhabitants are Muslims.

Niger notified the first cases of acquired immunodeficiency syndrome (AIDS) in 1987. Until the end of 2000, the cumulative numbers of notified AIDS cases was 5598 (UNAIDS/CEA 2000). Several studies have documented the spread of the epidemic (Decroix & de Saint Martin 1990; Ousseini *et al.* 1991, 1995; Gragnic *et al.* 1998; Mamadou *et al.* 2002). HIV infection is monitored through sentinel surveillance targeted mainly at pregnant women and female sex-workers. HIV surveillance information is available from 1988. In 2001, the seroprevalence among pregnant women ranged from 1.4% to 5.5%, according to study sites, with an average prevalence estimated at 2.8% (T. Sanda Aksenenkova, unpublished data). The Working Group on Global HIV/AIDS and STI surveillance, associating the Joint United Nations Programme on HIV and AIDS (UNAIDS) and the World Health Organization (WHO), estimated that 61 000 adults aged 15–49 years (1.35%) were living with HIV/AIDS at the end of 1999 (UNAIDS/CEA 2000), while another document estimated the prevalence at 1.83% at the end of 2001 (Walker *et al.* 2003).

The seroprevalence of HIV infection among pregnant women is supposed to represent a relevant estimate of the seroprevalence in the general population of adults. However, this is subject to some biases, such as the representativeness of women attending antenatal clinics (ANC). The only way of assessing precisely the prevalence of HIV among the whole general population and of calibrating the results of the routine surveillance system consisted in conducting a survey especially designed to achieve this goal.

Population and methods

Ethical aspects

The study was commissioned by the Ministry of Health of Niger and reviewed and approved by Niger's *Comité National Consultatif d'Ethique*.

We approached randomized individuals and explained the methods and aims of the survey, with unequivocal reference to HIV testing, but pointed out that the study design did not generate individual results. Informed oral consent was obtained from study participants, and we also outlined the procedure implemented in Niger for free voluntary anonymous HIV testing and counselling to individuals who wished to know their HIV status.

Sampling method

A representative sample of the general population aged 15–49 years was drawn using a two-stage cluster sampling design. Reference population data were those of the Third General Population and Housing Census (3e RGPH) performed in May 2001 (unpublished data) which divides the total population into about 9000 basic units making up 42 districts that constitute eight regions. As a first step, after having stratified the region and the type of settlement (rural *vs.* urban), we randomized 120 basic units of population according to the method of cumulative numbers of population. For a given region, the number of randomized basic units was proportional to the population size. As urban population accounted for less than 20% of the total population of the country, and to ensure that confidence intervals of prevalences would be narrow enough, the sampling fraction used for urban areas was twice as big as the one used for rural areas. The second step consisted of a randomization of households after having performed their counting. The composition of households was not available, but was known to be very heterogeneous due to the high frequency of polygamous families. Randomized households were visited until we had enrolled 25 men and 25 women. Every member of a randomized household was invited to participate and refusers were not replaced. All individuals living in the last household falling into the sample were included so that the cluster size could exceed 50 persons.

Data collection

Every adult aged 15–49 years, living in a randomized household, was asked to answer questions about demographic data, education level, occupation, marital status, history of blood transfusion or surgery. The standardized questionnaires were filled in by the investigators. As collected data had to be anonymous and unlinked, only a code number was used to identify study participants so that the results could not be traced back to individuals.

Blood collection was performed by finger pricking on Serobuvard® (LDA22, Ploufragan, France) filter paper using sterile disposable safety lancets. Six pre-punched calibrated spots of 7 mm diameter each were collected from each individual. The blood spots were left to dry at ambient temperature for about 4 h and then placed in paper envelopes. At the arrival at the CERMES (Niamey), the dried blood spots (DBS) were stored in plastic sealed bags at +4 °C until use.

Laboratory method

All blood specimens were tested at CERMES (Niamey) according to an algorithm defined by this laboratory for the purpose of the study (O.N. Ouwe Missi Oukem-Boyer *et al.*, unpublished data). The strategy is slightly different from UNAIDS testing strategy II (WHO 1997). Briefly, after elution of blood from DBS, the specimens were first tested with Genscreen® HIV 1 + 2 kit (Biorad), whose sensitivity on Nigerien positive controls was found to be 100%. Negative specimens were then definitely considered as corresponding to non-infected individuals. Positive specimens were further tested using Vironostika® HIV Uniform II plus 0 (Organon Teknika) and negative results with this test were considered as definitive while positive results were later tested with Immunocomb® II Bispot HIV-1 & 2 (Orgenics). Specimens found negative for Immunocomb were considered as definitively negative.

Quality control was performed at the Centre Pasteur of Cameroun (Yaoundé) and at the Institut Pasteur of Central African Republic (Bangui). Each centre was sent 30 DBS specimens including 20 negative and 10 positive. The two laboratories were blinded to the results from the CERMES.

Data analysis

Data analysis was performed using Epi-Info and SPSS statistical softwares. The 95% confidence intervals of seroprevalence were calculated taking into account the actual value of the cluster design effect computed from observed data. The estimated numbers of HIV-positive individuals in 2002 were computed after having updated the 2001 population size with an estimated 3.3% growth. For statistical analysis, the Pearson's chi-square test, the adjusted Mantel–Haenszel's test and the Kruskal–Wallis anova were used whenever appropriate. A P-value < 0.05 was considered significant. Possible interactions between risk factors were tested, particularly interaction with the modalities urban/ rural of the variable 'environment'. The comparisons between crude ORs and adjusted ORs have been done to look for possible counfounding effects.

The multivariate analysis of the risk of being tested positive for HIV according to explanatory variables thought to be potentially interesting was performed using a logistic regression. The gender was expressed as a binary variable coding with 0 representing males and 1 representing females. The age with four categories was recoded in terms of three dummy variables. Past transfusion and history of surgery were each coded as binary variables 1/0. The environment was expressed as a binary variable coding with 1 representing urban areas and 0 representing rural ones. The educational level was recoded as two dummy variables coding for three levels: never attending school, primary/other (including Koranic) and secondary/higher. The marital status was recoded as two dummy variables coding for three levels: single, married (either monogamous or polygamous) and formerly married (widowed or divorced). A backward stepwise procedure was used to identify the predictors of HIV seropositivity; removal testing was based on the probability of the likelihood ratio statistic. The goodness of fit of the model was assessed using Hosmer and Lemeshow's goodness of-fit statistic.

Results

The survey was conducted between May and July 2002. All randomized communities could be reached. Of 6128 valid records from 6140 randomized individuals, 65 (1.1%) showed either partial or complete refusal. A total of 6056 blood specimens were suitable for testing. The male-to-female ratio was 0.98 (0.99 and 0.96 for country people and city-dwellers, respectively). The mean ages were 26.6 years for females and 28.6 years for males.

A total of 68 blood specimens were positive for HIV antibodies. No indeterminate result was observed. Among rural individuals, 26 were HIV positive (0.64%; 95% CI, 0.35–0.94%), of whom 25 were infected by HIV-1 and 1 by HIV-2. The seroprevalence was significantly higher in urban areas as 42 of 2019 tested individuals (2.08%; 95% CI, 1.20–2.96%) were positive: 40 for HIV-1, 1 for HIV-2 and 1 presented a dual infection by HIV-1 plus HIV-2. For the whole country, the adjusted estimate of HIV prevalence was 0.87% (95% CI, 0.5–1.3%), taking into account the actual distribution of the population between rural areas (84%) and urban areas (16%).

In rural areas, the prevalence was 0.7% in females (95% CI, 0.3–1.1%) and 0.6% in males (95% CI, 0.3–0.9%) while in urban areas it was 2.6% in females (95% CI, 1.3–3.9%) and 1.5% in males (95% CI, 0.7–2.3%). The age- and sex-specific prevalence rates for urban and rural populations are shown in Figure 1.

Considering the 2002 population size, the 95% CI of the estimated total number of HIV-positive individuals was (22 864–59 640). The intervals for rural and urban population were (13 952–37 472) and (8911–22168), respectively.

In addition to environment urban/rural, in univariate analysis HIV positivity was significantly associated with age-group, family situation and history of surgery (Table 1). There was no significant interaction between environment and the three other variables. The comparison between crude and adjusted odds ratios was not evocative of any counfounding effect.

Using logistic regression analysis, the variables significantly related to the risk of being tested positive for HIV were age, marital status and environment urban/rural (Table 1). The goodness-of-fit chi-square was 4.3 with 7 degrees of freedom (NS), indicating that the values predicted by the model were not significantly different from the observed data.

The results of the 60 DBS specimens tested for quality control in Bangui and in Yaoundé were 100% in agreement with those obtained at the CERMES.

Discussion

Large serosurveys in tropical developing countries usually come up against strong difficulties, including lack of updated population data and logistical constraints imposed by poor road networks, inadequate means of communication and high temperatures. As Niger had carried out a national census in 2001, reliable data on population size and distribution were available, allowing for good randomization. The refusal rate was much lower than the expected 5%. The method of blood sample collection probably had a decisive impact on acceptability. The use of DBS for HIV serosurveillance had been already recognized as simple and inexpensive (Boillot *et al.* 1997) and its suitability for large HIV serosurveys is indisputable, especially in remote tropical areas where storing total blood samples or serums for several days may be tricky. Furthermore, investigators

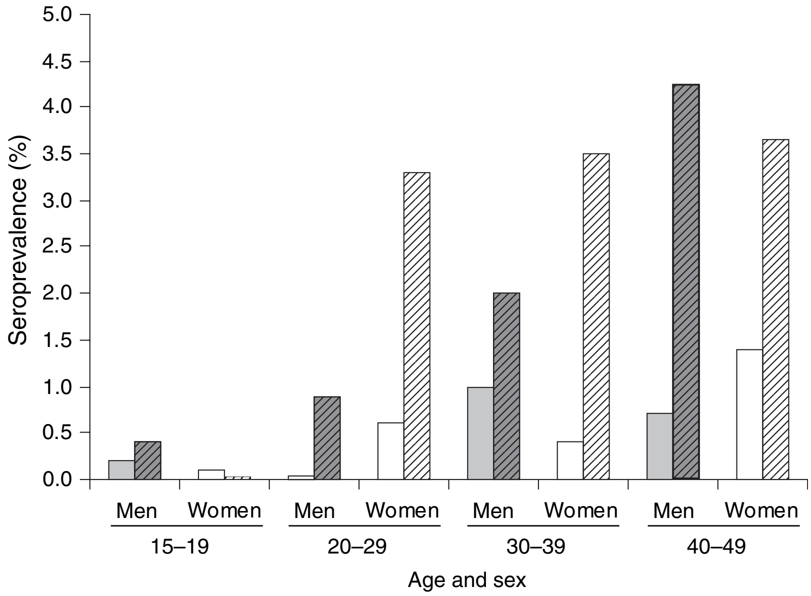

Figure 1 HIV seroprevalence according to sex and age in urban and in rural areas (striped bars: urban).

with experience of that kind of study reported that safety lancets seemed to be better accepted than standard blood lancets.

Surveillance of HIV infection through women attending ANC may lead to biased estimation (Neequaye *et al.* 1997; Fylkesnes *et al.* 1998), and indeed the adjusted

Table 1 Distribution of the main variables and their association with HIV sero-positivity

	Univariate analysis			Multivariate analysis		
Variables	*n*	OR	*P*-value	OR	95% CI	*P*-value
Gender						
Male	2988	1.00		1.00		
Female	3062	1.49	0.11	1.42	0.83–2.43	0.19
Age (years)						
15–19	1443	1.00		1.00		
20–29	2250	5.18	0.002	5.11	1.47–17.67	0.01
30–39	1407	7.62	0.0001	7.94	2.13–29.59	0.002
40–49	956	9.73	0.00000	9.85	2.54–38.25	0.001
Environment						
Rural	4037	1.00		1.00		
Urban	2019	3.28	0.00000	3.08	1.83–5.18	0.0000
Marital status						
Married	4233	1.00		1.00		
Single	1661	0.68	0.23	1.17	0.52–2.62	0.70
Ex-married	158	6.96	0.00000	4.63	2.28–9.38	0.0000
Surgery						
No	5920	1.00		1.00		
Yes	132	3.66	0.016	2.14	0.82–5.58	0.12
Educational level						
Secondary/University	890	1.00		1.00		
Primary/other	2039	0.61	0.14	0.81	0.39–1.66	0.57
Never attending school	3113	0.61	0.11	0.79	0.38–1.67	0.55
Blood transfusion						
No	5898	1.00				
Yes	154	1.78	0.33	Not tested		

seroprevalence found in our study is appreciably lower than the value estimated from pregnant women surveillance (2.8% in 2001, T. Sanda Aksenenkova, personal communication). At least two reasons can explain the discrepancy with the prevalence obtained from ANC surveillance. First, it is not sure that pregnant women are fully representative of the general adult population in all countries. Some local customs, regarding marriage for example, might have lead to specific epidemiological patterns. The second reason is the representativeness of sentinel sites. In Niger, as in other countries with few laboratory resources, surveillance sites are more often implemented in urban areas. In 2001, of the 10 sites involved in ANC surveillance, six were located in main towns. The four others that were supposed to represent rural populations were located in smaller towns which cannot be considered as truly rural areas. Furthermore, although urban populations comprise less than 20%, the national estimate was not computed by weighting urban and rural values. Actually, the prevalence assessed from ANC (2.8%) was not so different from the prevalence among urban women assessed from the population survey (2.6%). In the future, a more sensible choice of ANC participating in the HIV surveillance, with accurate representation of rural populations, should significantly improve the accuracy of data.

The very low seroprevalence observed in young adults is worthy of note. The survey did not tackle behavioural aspects, but the results of the Demographic and Health Survey (EDSN-II) carried out in 1998 can help to venture a hypothesis. According to this survey, 36.5% of women aged 15–19 years had never had sexual intercourse, compared with 74.1% of young men in the same age-group, and 33.7% in the 20–24 age-group (Attama *et al.* 1999). Furthermore, in almost all couples, the husband was older than the wife: the difference was ≥15 years in 21.3%, it was between 10 and 14 years in 25.3% and between 5 and 9 years in 16.2%. On average, husbands were 10.1 years older than their spouses. This observation may explain, at least partly, why the prevalence is low among young male adults and why women are infected earlier than men.

Although the association between gender and HIV positivity was not statistically significant, may be because of an insufficient number of positive individuals in our sample, women account for about 60% of seropositive individuals in Niger, in accordance with observations made elsewhere in Sub-Saharan Africa (WHO 2002). Since the first AIDS notifications made by Niger, the male-to-female ratio of seroprevalence reversed and males who represent about 70% of the cumulative number of AIDS cases (UNAIDS/WHO 2002) account now for about 40% of infected individuals. Since the beginning of AIDS notifications, no case was reported as being related to homosexual contact between men and it is unlikely that changes in the male-to-female ratio of prevalence would be because of changes in respective importance of modes of transmission. Many Nigerien, usually males, have seasonal employment in southern coastal countries for several months a year and they could have contributed to a significant proportion of the first cases. The current proportion of females in infected individuals is an indicator of worsening in the course of the epidemic.

Compared with surrounding nations, Niger has not been affected too badly by the HIV epidemic (UNAIDS/WHO 2002). Only Mali, with a prevalence of 1.7%, was nearly comparable. We cannot explain this relatively low seroprevalence rate in Niger, but it is likely that the high proportion of rural population (84%) and the low population density play a significant role. For the rest, comparative behavioural surveys should be carried out. While many African countries are faced with hundreds of thousands of HIV-positive persons, the number of infected individuals in Niger makes projects to promote access to potent antiretroviral therapies for the majority more realistic. Furthermore, the implementation of these projects will probably motivate some people to undertake HIV testing, contributing to enhance both disease surveillance and prevention.

Although reassuring, the results of this survey must not lead to complacence. First, the incidence of HIV-infections is unknown and we have no accurate idea about the trends of the epidemic in the country. The recent history provided examples of nations where the HIV epidemic has soared within a short time. Secondly, the seroprevalence is not homogeneous and recent surveys in female sex-workers have demonstrated that this group suffers very high seroprevalence rates, representing a strong epidemiological risk.

As population-based serosurveys are expensive and difficult to conduct, they are not recommended by the UNAIDS/WHO working group as a routine part of serosurveillance (UNAIDS/WHO 2000). We fully agree on this point, but we believe that such surveys repeated, by example, every 5 years would represent the most reliable way of assessing the evolution of the HIV epidemic in a country, particularly if sample sizes are computed to ensure narrow confidence intervals. The result of the present survey will be therefore the reference baseline of the HIV situation in Niger.

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