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Human African trypanosomiasis amongst urban residents in Kinshasa: a case-control study

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Summary

BACKGROUND Increasing numbers of human African trypanosomiasis (HAT) cases have been reported in urban residents of Kinshasa, Democratic Republic Congo since 1996. We set up a case-control study to identify risk factors for the disease.

METHODS All residents of the urban part of Kinshasa with parasitologically confirmed HAT and presenting for treatment to the city's specialized HAT clinics between 1 August, 2002 and 28 February, 2003 were included as cases. We defined the urban part as the area with contiguous habitation and a population density >5000 inhabitants per square kilometre. A digital map of the area was drawn based on a satellite image. For each case, two serologically negative controls were selected, matched on age, sex and neighbourhood. Logistic regression models were fitted to control for confounding.

RESULTS The following risk factors were independently associated with HAT: travel, commerce and cultivating fields in Bandundu, and commerce and cultivating fields in the rural part of Kinshasa. No association with activities in the city itself was found.

DISCUSSION In 2002, the emergence of HAT in urban residents of Kinshasa appears mainly linked to disease transmission in Bandundu and rural Kinshasa. We recommend to intensify control of these foci, to target HAT screening in urban residents to people with contact with these foci, to increase awareness of HAT amongst health workers in the urban health structures and to strengthen disease surveillance.

keywords human African trypanosomiasis, urban, case-control study, risk factors, Democratic Republic of Congo

Introduction

Since the early 1990s a resurgence of sleeping sickness has been observed in the Democratic Republic of Congo (DRC) (Van Nieuwenhove *et al.* 2001). Urban centres seem not to be exempt. The Province of Kinshasa reported more than 2400 human African trypanosomiasis (HAT) cases between 1996 and 2000, peaking at 912 in 1999 (Bilengue *et al.* 2001). Ebeja *et al.* (2003) reported that 39% of the 2451 cases were urban residents. In 2001 686 cases were observed in the same province and 459 in 2002 (Ebeja *et al.* 2003). HAT has always been considered a rural problem (Laveissiere *et al.* 1994) although there are some reports on urban HAT. Noireau *et al.* (1987) mentioned two cases who had reportedly been infected in urban Brazzaville. Urban transmission has nevertheless not been confirmed. Although Gouteux *et al.* (1986) observed tsetse flies in the national park at the centre of Brazzaville, they could not confirm that these were *Trypanosoma brucei gambiense* infested (Gouteux *et al.* 1987). In Ivory Coast, Fournet *et al.* (2000) demonstrated that urban cases in Daloa had been infected in the surrounding plantations. So far, there is no confirmation of local transmission in urban Kinshasa. As HAT is endemic in the neighbouring provinces of Bandundu and Bas Congo, importation of cases is plausible. But in colonial times, areas close to the present city were well-documented HAT foci (Burke & Janssens 1992), and recent entomological surveys have repeatedly found tsetse flies in peri-urban areas of Kinshasa (Mulumba *et al.* 1993; Watsenga & Manzambi 1998; Ebeja *et al.* 2003).

Two major questions arise from these observations: Can *Glossina* spp. adapt to an urban environment or enter town in sufficient numbers, and if so, what is the risk of urban HAT transmission? And what are the appropriate control strategies for HAT in a megalopolis such as Kinshasa? The latter question remains valid even if all urban cases would prove to be imported. For rural areas, standard control strategies are repeated rounds of active population screening combined with passive case detection in the health structures and epidemiological surveillance (Van Nieuwenhove 1991; World Health Organisation 1998). However, in densely populated urban Kinshasa it would take 88 mobile teams to screen the population once a year (Bilengue *et al.* 2001), which is clearly not feasible. Bilengue *et al.* (2001) proposed vector control along the rivers crossing Kinshasa and in the vegetable gardens surrounding Kinshasa and training of first line health workers to detect cases. Ebeja *et al.* (2003) suggested serological screening of all patients presenting to the city's primary health care structures and targeting of specific risk groups. To appraise which of these strategies, if any, are appropriate in this urban environment, we need a better understanding of the risk factors for acquiring HAT amongst the population from the urban part of Kinshasa. Therefore, we set up a case-control study to identify these factors.

Methods

Study area and background

The province 'Ville de Kinshasa' has a surface area of 10 000 km^2. Population estimates vary between 5.273 million (source: Institut National de Statistique de la République Démocratique du Congo, Rapport 1984, unpublished data) and 7 million. The largest part of the province has a rural ecology whilst the urban zone is limited to 450 km^2 stretched along the river Congo (see Figure 1). This urban zone consists of two parts: the inner city is surrounded by a peri-urban belt of what used to be villages but is now contiguous habitation spotted with vegetable gardens on small irrigated plots (Ebeja *et al.* 2003). The western part of the inner city contains a large residential area with a lot of vegetation. The urban health system comprising government and private facilities is organized in 22 health districts ('zones de santé'), receives inadequate funding and functions poorly. Treatment for HAT in Kinshasa is offered in four specialized centres (Centre de Diagnostic, Traitement et Contrôle Maluku, Centre Hospitalier Roi Baudouin, Centre Neuro-Psycho-Pathologique of the University of Kinshasa and Kikimi Health Centre). The national HAT control programme (Programme National de Lutte contre la THA) provides the necessary supplies and these four centres are the only locations where HAT drugs are available. The specific drugs for HAT treatment are free of charge.

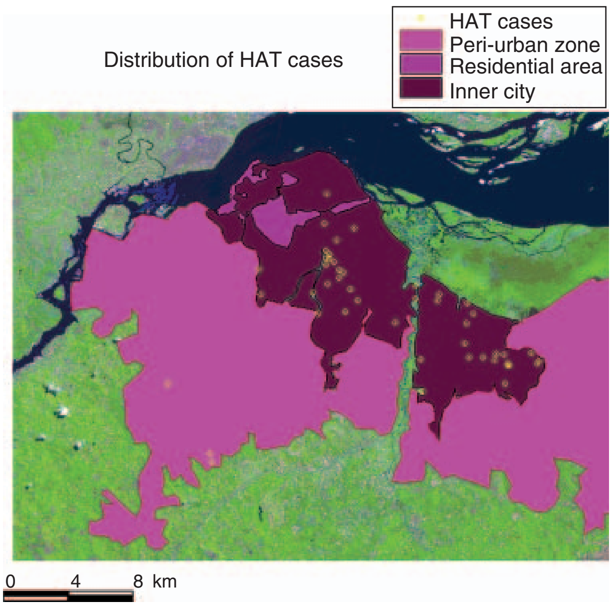

Figure 1 Distribution of 50 HAT cases in the urban part of Kinshasa, August 2002–February 2003.

Recruitment of cases

We included all HAT cases in urban residents that presented for treatment to one of the four specialized centres between 1 August, 2002 and 28 February, 2003. Inclusion criteria were: to be a parasitologically confirmed case and having been resident in the urban part of Kinshasa for more than 2 years. We defined the urban part as the perimeter with contiguous habitation (in contrast with the rural zone, where the habitation is organised in villages) and a population density above 5000 inhabitants per square kilometre.

Recruitment of controls

We identified two controls for each case matched on age (within 10 years), sex and neighbourhood. The study team went to the address of the HAT case and recruited controls in the same street, going from house to house starting from the nearest end of the street, until two controls could be enrolled. To rule out infection, each control was tested with the card agglutination test for trypanosomiasis (CATT; whole blood) (Magnus *et al.* 1978).

Interview

A structured interview was used to collect information on economic and household activities, travel history and exposure to known HAT foci. The head of the treatment centre or of the mobile team conducted the interviews of the cases. One of the investigators interviewed all controls and, where possible, reinterviewed the cases as a quality check.

Sample size

We expected to enrol 80 HAT cases and 160 controls within 6 months. With this sample size the study had 80% power (alpha error 5%) to detect a risk factor with an odds ratio of 3 or more that is present in at least 10% of the non-exposed, assuming a phi-coefficient up to 0.2 (Dupont 1988).

Geographical information system (GIS)

An in-depth study of HAT in Kinshasa requires a clear demarcation of the different ecological zones in and around the city, but a precise digital map of the area was not available prior to the study. Therefore we selected a multispectral satellite image of Kinshasa among the archive images of the SIRIUS database (http://sirius.spotimage.fr). The coloured image (SPOT 4 – multispectral mode XI), dated 2 April, 2002 covers an area of 60 km × 60 km and has a pixel resolution of 20 m. After converting and resampling of the satellite data, a colour composite image of bands 2, 3 and 4 was produced using IDRISI software (Clarks Labs, Clarks University, Worcester, MA, USA) and imported as a bitmap file in Arcview GIS 3.2 (Environmental Systems Research Institute, Redlands, USA). We recorded the geographical coordinates of the residence of each case using a hand-held 12-band global positioning receiver Garmin (Garmin Ltd, CA, USA) likely to be accurate to approximately 15 m. These data were imported into the ArcView GIS database and displayed on the digital map.

Data analysis

The epidemiological data were entered in EPI INFO format (version 6) and analysed using EPI-INFO and STATA. In univariate analysis we calculated matched odds ratios with confidence intervals using the Mantel–Haenszel method. Exposures with more than one level were analysed using conditional regression for matched data. Subsequently we fitted a conditional regression model for matched data, building it with an anterograde method including exposures of interest that were significantly ($P < 0.2$) associated with disease in the univariate analysis. The contribution of each variable to the model was tested with the likelihood ratio test (significance level $P < 0.05$).

Ethical aspects

We explained the objectives and methods of the study to every potential participant and asked them to sign a written informed consent statement in the local language prior to enrolment. If the participant was a minor, consent was obtained from the parent or guardian. The Institutional Ethical Review Board of the Institute of Tropical Medicine of Antwerp and of the Ministry of Health of the DRC approved the study protocol.

Results

Between 1 August, 2002 and 28 February, 2003 we detected and included 50 eligible cases and 100 controls in the study. One control was subsequently found CATT-positive and excluded from the analysis. A total of 47 cases came from the urban zone, three came from the peri-urban zone. The map shows the residence of the cases.

Table 1 shows the characteristics of cases and controls. They were matched on age and sex and comparable with regard to level of education. Most cases (94%) were in the second stage of the disease and detected through passive case finding (82%). All cases resided for at least 2 years in urban Kinshasa, six cases moved from outside urban Kinshasa in the last 10 years.

Table 2 shows an overview in univariate analysis of all potential risk factors. There were very strong and significant associations with cultivating fields in rural Kinshasa, commercial activities in rural Kinshasa, with

Table 1 Characteristics of cases and controls

	Cases (n = 50)		Controls (n = 99)	
	n	%	*n*	%
Sex				
Male	23	46	45	45
Female	27	54	54	55
Highest level of education reached				
No education	6	12	8	8
Primary school	10	20	18	18
Secondary school	31	62	66	67
Higher education	3	6	7	7
Age group (years)				
0–20	13	26	25	25
21–30	9	18	27	27
31–40	18	36	27	27
>40	10	20	20	20
Stage of the disease				
First	3	6	NA	
Second	47	94	NA	
Mode of detection				
Active	9	18	NA	
Passive	41	82	NA	

HAT, human African trypanosomiasis; NA, not applicable.

Table 2 Risk factors for acquiring HAT in urban residents of Kinshasa (2003), univariate analysis

	Cases (n = 50)		Controls (n = 99)				
	n	%	n	%	OR	CI	P-value
Commercial activities							
In urban Kinshasa	9	18	20	20	2.8	0.8–9.6	0.1
In rural Kinshasa	10	20	2	2	20.3	3.5–117	<0.001
Outside Kinshasa province	9	18	14	14	3.1	0.8–11.5	0.1
Cultivating fields							
In urban Kinshasa	3	6	11	11	0.7	0.2–3.2	0.7
In rural Kinshasa	10	20	1	1	31.1	3.7–264	<0.01
Outside Kinshasa province	12	24	10	10	4.4	1.5–12.9	<0.01
Raising livestock	10	20	8	8	3.3	1.0–17.8	0.06
Fishing	8	16	10	10	2.01	0.54–7.17	0.37
Working at fish ponds	2	4	2	2	0.75	0.01–15.6	0.68
Travelled in the past to							
Places in Kinshasa province							
Maluku	32	64	45	45	2.61	1.11–7.35	0.028
Buma	6	12	3	3	5.38	0.89–54	0.08
Chute Lukaya	9	18	26	26	0.56	0.16–1.5	0.30
Nganga Yala	3	6	0	0	0.57	0.09–3.01	0.81
Ma Vallée	2	4	10	10	0.26	0.03–1.93	0.28
Ndjili (valley)	4	8	21	21	0.32	0.05–0.98	0.055
Kinkole	9	18	22	22	0.75	0.26–2.03	0.70
Other provinces							
Bandundu	32	64	30	30	10.18	3.01–53	<0.0001
Equateur	14	28	14	14	3.07	1.09–9.46	0.048
Bas-Congo	17	34	42	42	0.56	0.27–1.50	0.36
Kasai occidental	10	20	14	14	1.55	0.39–4.83	0.77
Kasai oriental	4	8	13	13	0.55	0.14–2.40	0.41
Maniema	2	4	4	4	0.75	0.01–15.6	0.68
Katanga	6	12	6	6	3.08	0.57–20.35	0.26
Abroad	10	20	23	23	0.77	0.30–2.14	0.82
River-related activities							
Bathing	23	46	56	57	0.43	0.19–1.26	0.18
Swimming	4	8	18	18	0.30	0.04–1.06	0.08
Washing clothes	20	40	20	20	3.2	1.3–10.4	<0.005
Taking water	13	26	6	6	3.2	1.1–8.9	0.02
Soaking of cassava roots	8	16	1	1	15.5	1.8–130	<0.001
Fishing	3	6	3	3	2.08	0.28–16.3	0.66
Other activities	2	4	22	22	0.80	0.11–4.08	0.89

HAT, human African trypanosomiasis; OR, odds ratio; CI, confidence interval.

soaking of cassava roots and with travel to the HAT-endemic province of Bandundu. The place most often quoted for commercial and agricultural activities in rural Kinshasa was Mai-Pembe, a known HAT focus situated 100 km to the east of the city. Associations with cultivating fields outside Kinshasa province, with travel to Equateur province and to Maluku, an endemic focus in rural Kinshasa, were less strong. Some activities performed near rivers, such as washing clothes and fetching water, were also associated with HAT.

In the final logistic regression model HAT in urban residents was associated with their exposure to the province of Bandundu and with commercial activities in rural Kinshasa. Three levels of exposure for travel to Bandundu showed increasing adjusted odds ratios: ever travelled to Bandundu, conducting commercial activities in Bandundu and cultivating fields in Bandundu. Conducting commercial activities and cultivating fields in rural but not in urban Kinshasa was associated with HAT (Table 3). We performed tests for interaction for all variables, but none were found.

Table 3 Risk factors for HAT in urban residents of Kinshasa, conditional logistic regression model for matched data

	OR	CI		*P*-value
Travel to Bandundu				0.0001
Travelled to Bandundu in the past	9.9	2.1	47	0.004
Commercial activities in Bandundu	20.5	1.5	278	0.02
Cultivating fields in Bandundu	116	10.2	1327	0.001
Commercial activities in Kinshasa				0.025
Urban	4.1	0.7	25	0.12
Rural	16.6	1.7	166	0.02
Cultivating fields in Kinshasa				0.067
Urban	1.3	0.3	6.8	0.75
Rural	9.2	0.9	89	0.06

HAT, human African trypanosomiasis; OR, odds ratio; CI, confidence interval.

Discussion

This study provides insight into the mechanisms that led to the reemergence of HAT in Kinshasa in the late 1990s. It shows that HAT in the city of Kinshasa is mainly linked to disease transmission in Bandundu province and rural areas of Kinshasa province. After cross-checking our data from the urban treatment centres with the surveillance data from the control programme, we are confident that we recruited almost all HAT cases detected in the study period. It is unlikely that an urban resident will seek HAT treatment outside Kinshasa, as distances are long and travel difficult. However, we doubt that all HAT cases in urban residents have been detected by the health services or the control programme during the study period. Anecdotal reports indicate that some true HAT cases end up with a wrong diagnosis such as AIDS, as the urban health workers are not often including HAT in their differential diagnosis. This could make us overestimate the association with known foci in Bandundu, and underestimate a possible association with exposure inside the urban perimeter. Indeed, people travelling to known HAT-endemic areas may be more risk-aware, and therefore more inclined to participate in screening sessions conducted by specialized mobile teams, hence be correctly diagnosed as HAT and have more chance to be included in our study.

Control status was ascertained by a serological test to rule out infection. Cases and controls were matched for sex, age and neighborhood. Matching may have caused an underestimation of the effect of certain variables linked to neighbourhood, such as social class or level of education. It is reassuring although that we found important differences in risk profile between cases and controls. Our data show that HAT in urban Kinshasa is mainly associated with agricultural activities in rural Kinshasa and outside Kinshasa province, commercial activities in rural Kinshasa and Bandundu and travel to Bandundu. We found no evidence for an association with activities in urban Kinshasa. Certain activities performed near the rivers were associated with a greater risk for HAT in the univariate analysis, especially the soaking of cassava roots. This activity was already mentioned as a risk factor by Van Hoof in his 1933 report on HAT in the Léopoldville area (Van Hoof & Henrard 1933). However, closer analysis revealed that the association was confounded by other risk factors. Indeed, soaking of cassava by urban residents is most likely performed on a commercial basis, and not as a regular household activity. The association with washing clothes and fetching water also disappeared after adjustment.

Case-control studies have been used before to assess risk factors for acquiring *T.b. gambiense* in Cameroon and Ivory Coast. Meda *et al.* (1993) found similar associations of HAT with visiting remote farms, trade in agricultural products and fetching of water. Grebaut *et al.* (2001) only found an association with hunting. However, they studied HAT risk factors in a rural environment and comparison with our study is difficult. Other risk factor studies were conducted in Uganda and Zambia on *T. b. rhodesiense* sleeping sickness (Okia *et al.* 1994; Fevre *et al.* 2001; Wyatt *et al.* 1985), but the epidemiology of the two diseases differs notably (Welburn *et al.* 2001). In the *T.b. gambiense* area, Fournet *et al.* (2000) found that HAT transmission did not occur in the town of Daloa (Ivory Coast) but in cash crop plantations in the peri-urban area.

Our study thus mainly shows a strong link with agricultural activities performed by the urban residents in rural Kinshasa and Bandundu. Instead of qualifying the problem as an urbanization of HAT, one could consider this an issue of ruralization of the city. Protracted civil war, continuing socio-economic decline and non-payment of wages in the public sector has much decreased employment in the formal sector in the capital. Ever more urban dwellers resort to agriculture-related activities as a source of income. Many commute on a daily basis to the rural areas surrounding the city, others stay for longer periods in the more remote places. This brings them in close contact with habitats of tsetse flies and may explain most of the current HAT cases. Commercial activities in rural Kinshasa, another strong risk factor, consists mainly of trade in agricultural commodities and patients may get infected while prospecting fields and in some cases harvesting the crops they purchased. Contrary to our expectations, we did not find an association of HAT with activities in the peri-urban belt, which in 2002 remained tsetse-fly infested. However, our data do not rule out that local transmission could have taken place there in 1998–1999 as suggested by Ebeja *et al.* (2003) on the basis of observed clustering of cases. Intensification of case finding and vector control efforts might have reduced or eliminated transmission since (Bilengue *et al.* 2001).

It follows from our results that control of the disease foci in rural Kinshasa and Bandundu will have the largest impact on the current number of HAT cases in urban residents of Kinshasa. The tsetse infested peri-urban belt of the city needs a strengthening of the HAT surveillance, as there is a risk of new outbreaks starting from imported cases. We suggest to start serological screening of all patients presenting to health centres in that area and active population screening by the mobile teams, prioritizing those areas were cases are declared. Establishing the Epidemiological Risk Index (ERI) (Laveissiere *et al.* 1994) in the peri-urban area of Kinshasa and the river valleys will further permit to evaluate transmission risk, identify areas where surveillance needs to be particularly close and to evaluate if vector control is an appropriate intervention. In addition, targeted screening of travellers to the risk areas could contribute to the control of the problem. Active case finding, with the CATT test, at the river ports of the Congo river (river transport is both used by persons going to the fields and by traders) or amongst truckers commuting to endemic areas are interventions that could be tested and evaluated with regard to feasibility, acceptability, efficiency and effectiveness. Finally, there is a need to increase HAT awareness amongst the health workers in the first and second line of the urban health system so that they suspect and refer more easily possible cases for diagnosis and treatment.

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