

## **Risk Factors of Human African Trypanosomiasis in Mbuji Mayi, Eastern Kasai Province, Democratic Republic of the Congo**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Authors ABM and JCBT designed the study. Authors MIWK and TK managed data collection and initial literature search. Author NKZB completed supplemental literature search. Authors EKM, PC, TK and NKZB managed the analyses of the study and the writing of the results, discussions and conclusion. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aims:** Our study is aimed at determining the risk factors of Human African Trypanosomiasis (HAT) in Mbuji Mayi, Eastern Kasai Province, Democratic Republic of the Congo.

**Study Design:** We used a case-control design with a ratio of 2 controls for every HAT case.

**Place and Duration of Study:** Our multidisciplinary research team collected primary data on cases of HAT patients treated at the Referral and Treatment Center of Dipumba in Mbuji Mayi in 2012 and on their controls of similar gender and age, living in Mbuji Mayi, but free of HAT infection.

**Methodology:** We analyzed data, using both descriptive and analytical statistical procedures such univariate and multivariate methods of logistic regression. The association between the different factors studied and HAT infection has been determined by estimating the odds-ratio (OR) with a confidence interval (CI) of 95% and a P-value of less than 0.05. We interviewed 180 subjects (60 cases and 120 controls).

**Results:** The 60 cases were predominantly male (male-female ratio of 2.2:1) with the majority (53%) in the age group of 20-40 years. Subjects in the age group of over 40 represented 28.3% of the patients. The same patterns were seen in the control group. The age of interviewees varies from 11 to 65 years. HAT cases reported drawing water from wells (16.7% vs 6.7%;  $P > .05$ ), walking along the river bed and in the peat lands (11.7% vs 9.2%;  $P > .05$ ) at a higher rate than controls. The HAT cases reported involvement in various activities that put them in much closer proximity with water sources: bathing (8.3% vs 6.6%;  $P > .05$ ), dishwashing and laundry (20% vs 37.5%), fetching household water (50% vs 24.2%;  $P < .0001$ ), cassava retting roots (1,7% vs 7.5%), diamond digging in the mines (51.7% vs 21.6%;  $P < .0001$ ), trafficking or buying diamond from diggers (13,3% vs 8.3% ;  $P > .05$ ).

**Conclusion:** Involvement in activities that connect with water sources increases the risk of acquiring HAT infection in Mbuji Mayi.

*Keywords: African Human Trypanosomiasis, risk factors, Mbuji Mayi, Eastern Kasai Province, Democratic Republic of Congo.*

## 1. INTRODUCTION

### 1.1 Goal and Focus

We investigated the risk factors of Human African trypanosomiasis (HAT) in Mbuji Mayi. This is the capital city of the Eastern Kasai province, one of the eleven provinces of the Democratic Republic of Congo (DRC). We focused on HAT because this disease is very devastating for its victims [1,2]; and it is also of a major concern for the global health community [3,4,5]. Additionally, its prevalence in the DRC is the highest among all the affected countries in Africa [2,5,6]. We focused on Mbuji Mayi which we view as a challenging post-colonial urban agglomeration [7] and also as an illustration of what many other cities, particularly in resource constrained countries in Africa, experience health wise in the face of their demographic growth and increasing squatter settlement. Their challenge is about how to satisfactorily tackle the various issues of their evolution and address the needs of their growing populations [7,8,9,10,11]. This city is well positioned to serve as an illustration of the new trend that has been seen in the epidemiology of HAT: Traditionally reported as

affecting mostly rural populations, HAT is now increasingly occurring in urban agglomerations. Despite this emerging shift, so far, maybe with the exception of the city of Kinshasa, there have not been studies carried out to investigate its risk factors in any of the Congolese urban agglomerations. We hope to shed some light on these factors and to instruct and support the efforts under way at the national and global levels to eliminate this scourge [2, 12].

### 1.2 HAT as a Global Concern

Also known as “sleeping sickness”, HAT is not just confined to the DRC; it is in fact a widespread disease that affects some thirty sub-Saharan African countries infected by tsetse flies [6]. Even if the epidemics of HAT have been a significant public health problem in the past [8] and even if globally the disease is reasonably well-controlled at present, according to Simarro et al. [13,14], there are still 7,000-10,000 cases reported annually in recent years [1]. Not to mention that this condition caused the loss of  $\approx 1.5$  million disability-adjusted life years (DALYs) in 2002 [3].

### 1.3 HAT as a Specific African Disease

HAT is concentrated in Africa where it is seen in its two forms according to the sub-species of trypanosome that is responsible for the disease. The acute form due to *Trypanosoma brucei rhodesiense* is geographically localized in the southern and eastern parts of Africa; and the chronic, insidious form due to *Trypanosoma brucei gambiense* is geographically encountered in the Western and central parts of Africa [5]. Most of the sleeping sickness cases are caused by *Trypanosoma brucei gambiense* [2]. According to CDC, over 95% of the cases of human infection are found in the DRC, Angola, Sudan, Central African Republic, Chad, and northern Uganda [2].

### 1.4 HAT in the DRC

The DRC is the country with the largest number of HAT cases [5,6], and with one of the most resource-constrained national health care infrastructures to address this challenge [6]. According to World Health Organization (2014), "in the last 10 years, over 70% of reported cases occurred in the Democratic Republic of Congo (DRC)" [12]. The DRC is the only country that has reported more than 1000 new cases annually and accounts for 83% of the cases reported in 2012 [12]. According to the National Program for the Fight against HAT (DRC), nine of the eleven provinces of the DRC are affected by the HAT. Additionally, this is the country where gross estimates put the exposed population at 13 million people, where less than 20% of those exposed are under active surveillance and where nearly 8,000 new infected patients are reported each year [2,15]. The 2012 report on the HAT epidemiological situation in the countries that are parts of the HAT platform (Central African Republic, Chad, Sudan, Uganda, Angola, RDC) shows that the DRC reported 84.4 per cent of the HAT cases, or 5969 cases on a total of 7,102 HAT cases reported in all these countries [15,16]. The report for the previous year of the same platform indicates that in late 2011, the DRC had reported 85% of cases (5,595 of a total of 6,599) among these countries i.e.  $\frac{3}{4}$  of global cases [15].

### 1.5 HAT as an Urban Phenomenon

Compounding this issue is that in the DRC, HAT is no longer exclusively present in rural areas; it has extended to the large cities. From 1997 to

1999, endemic cases of HAT have been reported in four Congolese towns: 351 cases in Matadi, 1,235 cases in Bandundu, 1,307 cases in Mbuji-Mayi and 1,571 cases in Kinshasa [17,18]. This is a clear rupture from HAT traditional presence in rural areas and its most dominant consideration as a disease affecting rural Africa [19-22].

### 1.6 Previous Studies on HAT in the DRC

We are not aware of any systematic investigation of the risk factors of HAT in the Congolese urban agglomerations. Most of the previous studies in the DRC have focused on various clinical, epidemiological and social dimensions of this disease. They include studies that have explored the social history of sleeping sickness in the Northern area [23], the health care-seeking behavior and diagnostic delays [24], its patterns in a rural community [25] knowledge, behaviors, practices and beliefs regarding HAT [26], the distribution of *Glossina fuscipes quanzensis* and its risk of transmission in the peri-urban area of Kinshasa [27], the toxicity of HAT medicines and barriers against community participation in HAT control [28], the characteristics of HAT in children [29] and HAT reemergence in the capital city of the DRC [30].

### 1.7 Justification of the Investigation

As shown above, HAT due to *Trypanosoma brucei gambiense* has been reported in various Congolese communities. The disease has prompted a number of studies aimed at gaining a better understanding of its configuration. However this disease has largely, with the exception of Kinshasa the Capital City of the DRC, received little attention in terms of exploration and comprehension of its risk factors in other urban communities. Yet these urban communities have been increasingly growing demographically, still with the majority of their population living in conditions and engaging in behaviors that expose their health to greater risk of acquiring and suffering from HAT or other tropical diseases. Without the existence of an active and systematic screening and without adequate knowledge of risk factors in such urban communities, HAT may go ignored by the urban patient and undetected by the health care system for months or years, thus leading to delayed diagnosis at a late neurological stage (meningitis-encephalitic) and thus making the condition difficult to treat [31,2]. HAT is a serious disease. It brings physical, mental and

intellectual disability. When its treatment is delayed, the chances of recovery without neurologic sequels are minimal. In the absence of adequate treatment, the patient evolves toward apathy, terminal sleeping cachexia, coma and death [31,32,33,34].

Active search for cases by the mobile teams has resulted in a considerable reduction in the prevalence rate of HAT in the Congolese provinces of Equateur and Kinshasa; however the prevalence level remains stagnant in the provinces of Bandundu and Kasai. Since 2001, the province of Kasai unfortunately has moved to the second worst rank (with an average of 2500 new cases of HAT each year on nearly 700,000 persons examined) among the areas known for their highest endemic level of HAT following Bandundu (which province has reported an average of 4800 new cases of HAT each year on less than a million of persons examined) [35,36].

The foregoing discussion underscores once again the need to examine the situation of the Congolese provinces that have the highest burden of HAT and to explore the risk factors at play in the configuration of HAT infection therein. In doing so, the focus ought to be placed on the most populated, most impoverished and most at risk communities of these provinces, these being relatively new cities that have emerged without adequate pre-planning, that have not received adequate resources to establish solid public infrastructures for water supply and waste disposal, and that have served as places of refugee resettlement following the outbreak of ethnic cleansing in the Katanga province. Our study explores the risk factors in a city that has several of the aforementioned characteristics and whose geography, landscape, health system and socioeconomic conditions have directly or not contributed to greater exposure of its inhabitants to the HAT scourge or to a delayed HAT diagnosis.

## 2. STUDY SETTING

### 2.1 Geography

The city of Mbuji-Mayi is the capital city of the eastern Kasai province; and it extends over an area of approximately 145.19 km<sup>2</sup>. It is located in the intertropical convergence zone, where it rains abundantly, with precipitation reaching approximately 1400 millimeters of water during the wet season. Two seasons are observed: a dry season, from May to September, and a rainy

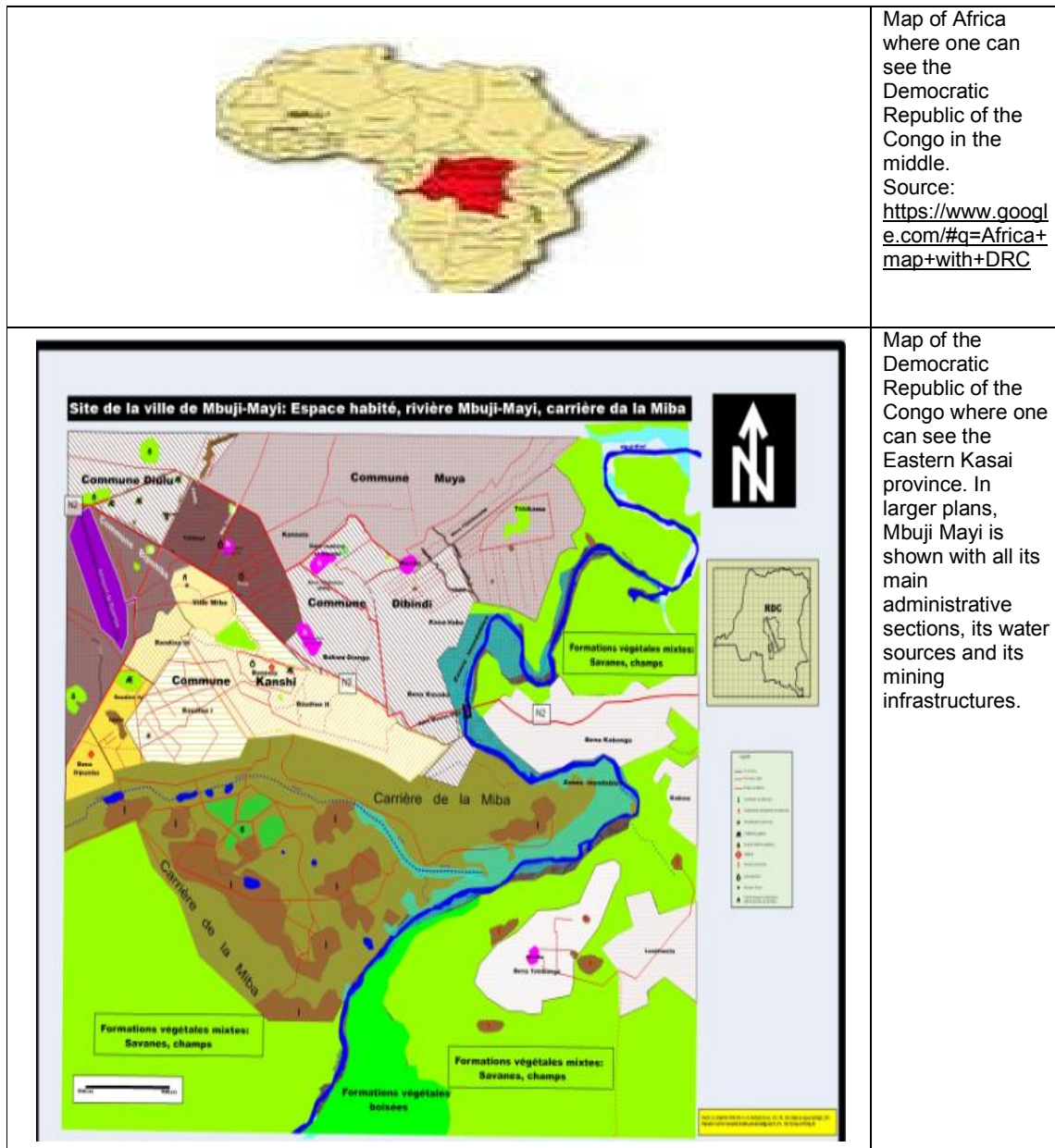
season, from October to April. The average annual temperature is 25°C [37]. The city of Mbuji-Mayi is a geographic area that extends between 6°5' and 6°10' of the south latitude and 23°27' and 23° 40' longitude east. It is located on the tray of the Kasai River, it is slightly hilly and it is distant by 930 km from Kinshasa, the capital of the DRC. As one can see from the map of the city (Fig. 1) [38], the site on which the city is built is drained by three rivers which constitute its natural limits. It is bordered to the north by the territory of Lupatapata and the Muya River, on the south by the Kanshi River, on the east by the Mbuji-Mayi River, which constitutes its border with the territory of Katanda, and to the west by a line joining the confluence Kanshi Nzaba to the Muya and Bipemba. The proximity of these water systems advantageously enables easy water supply for city dwellers, but it comes also as a liability by being the most suitable biotope for the vectors of diseases such as tsetse flies and mosquitoes which multiply and then breed on the same dwellers [39].

### 2.2 Population

Mbuji-Mayi is the third largest city in the country, following the capital Kinshasa and the second largest city Lubumbashi but ahead of Kisangani and Kananga. Its exact population is not known. In the absence of recent census, one can refer to the estimates that have been made recently by three different sources: The 2010 CIA Factbook offers the lowest estimate of 1,480,000 inhabitants [40]; the National Institute of Statistics (INS) gives its estimate of 1,900,000 inhabitants [41]; and the United Nations offers the highest estimate which places the population of the city at the highest level with 3,500,000 inhabitants [42]. The human population is formed by Pygmies and Bantus. While Pygmies form a minority that is confined to some districts in the Eastern Kasai province, Bantus represent the majority of the inhabitants of Mbuji Mayi. They are a mosaic of ethnic groups where the main groups are the Baluba, Tetela, the Songye and Kanyoka. The most spoken languages are Tshiluba, Lingala, Swahili, Tetela and French [43].

### 2.3 Health Organization

From a health organization perspective, the city is divided into 10 urban health zones [35,44]. The city serves as headquarter of the provincial coordination of the fight against HAT for the Eastern Kasai province.



**Fig. 1. Maps of Africa, of the Democratic Republic of the Congo and of Mbuji Mayi**

The center of reference and treatment of the HAT-Dipumba (CRT-DIPUMBA) is located in the compound of the Dipumba hospital in Mbuji-Mayi. This is within the area served by the health zone of Bonzola [2].

**2.4 Socioeconomic and Living Conditions**

To adequately grasp the paucity and extent of severity of the socioeconomic conditions of the inhabitants of Mbuji Mayi, one needs to be aware of some key elements of the rich and complex

political history of the DRC before and after Independence, particularly the history of the city, the discovery of diamonds in 1907, the social dynamics surrounding the industrial and artisanal production of diamonds in the DRC, and the successive politically motivated waves of forced displacement which have been characterized by the arrival and settlement of large numbers of internally displaced persons (IDPs) in or around the initial urban site.

#### **2.4.1 Early development of Mbuji Mayi**

The region where the city of Mbuji-Mayi now stands was once a cluster of villages on land owned by the Bakwanga clan [45]. According to Wong, “diamonds were first discovered in the area as early as 1907, but the true value of the find wasn't recognized until 1913 [45]. Following the discovery, a mining company known as “Société minière de Bakwanga” (MIBA) was formed. This new company built a mining camp designed to house miners and company officials in the area [45,46]. The young city grew quickly, but around strict planning by MIBA, which divided the community into labor camps, mining areas and living quarters. The city's growth was not explosive, and planning was done with the needs of the mining company in mind - not the development of the region as a general population center [45,46]. In fact, fearing theft of the company's diamond resources, the MIBA actively discouraged build-up in the region and closely monitored who went in and out of the region. Every person in the region needed a permit allowing them to be there, and registration at a command post that monitored the population, which made indefinite residence in the area almost impossible to establish [45,46]. There was limited economic activity besides the company-run mining, with even limited agriculture, and the city's population remained low, at approximately 39,830 by the late 1950s [46].

#### **2.4.2 Growth of Mbuji Mayi**

Mbuji-Mayi grew rapidly upon Congolese independence in 1960 with the immigration of many members of the Luba ethnic group from different parts of the country where, for political reasons, they were no longer welcomed to reside. Two waves of forced displacement brought a significant number of IDPs to the city. The first significant wave took place in the early 1960s. In the early 1990s, another wave broke out in the Katanga province [47,48]. Contrary to the persecution of the early 1960s stemming out of secessionist and separatist pursuits [49,50], this new crisis evolved from a power struggle between President Mobutu and the internal political opposition that sought to end his regime peacefully [51,52,53,54]. Mobutu undertook to divide the political opposition to politically weaken Etienne Tshisekedi, a politician of Luba Kasai origin named by the National Sovereign Conference as Prime Minister-elect responsible for leading the transition [52]. Between 1991 and

1995, successive waves of Kasaiian survivors left the Katanga province and arrived in the Eastern Kasai province and in other communities in the Western Kasai province. The conditions of destitution and overcrowding of these newcomers in the Eastern Kasai province were decried by many, prompting the provincial authority to engage in consultation with the Mbuji Mayi's mayor and to make the decision to resettle the newcomers on a vacant open land on the city's outskirts [55,56]. This initiative gave birth to a new community first called Cibombo and later renamed Cibombo Cimuangi - - Cimuangi is a Luba term which stands for “displacement” - - to make a clear distinction from the pre-existing village of Cibombo: Mobutu had succeeded in generating ethnic violence against Luba people in the Katanga province and in making Mbuji Mayi to grow again demographically well beyond the limited capacity of its infrastructure to provide the basic amenities of urban living. Like many of the previous settlers they have found in the city, these newcomers face a host of negative life prospects. Many engage in informal diamond digging as MIBA could only recruit and support a limited workforce.

#### **2.4.3 MIBA and employment prospects**

As the only mining company still in operation in Mbuji-Mayi up to its almost complete shutdown in 2008, MIBA was one of the main engines of the economy in a city where a very big proportion of the population, estimated at 3,5 million inhabitants, depends directly or indirectly on the extraction of the diamond. In 2004, MIBA however employed only 5700 people [57]. The rate of unemployment is estimated to be at least 90% [58]. A report entitled “*Diamants et Droit au Travail, Kasai Oriental, RDC*” and issued in 2009 by a partnership of human rights organizations in the DRC regarding the rights of mining workers in the Eastern Kasai province deplores not only the high level of unemployment in the province but also the prevailing very poor working conditions in the mines. These poor conditions have an adverse impact on the well-being of the families of the mining sector workers and the overall population of a city that depends mostly on the support coming from MIBA [58]. More disturbing is that most of the holders of these few jobs don't even enjoy just and favorable conditions of work in compliance with the stipulations of Article 7 of the International Covenant on Economic, Social and Cultural Rights (ICESC) [59].

#### **2.4.4 Work and working conditions outside MIBA**

Outside of MIBA, there are few other employment opportunities. The most important sector where people in Mbuji Mayi work is artisanal diamond mining. Following the liberalization of the mining sector in 1981, many of the dwellers of Mbuji-Mayi have abandoned the farming sector and even the schools to embrace artisanal diamond digging. Yet this liberalization was accompanied neither with regulations nor with adequate protection for these workers [58]. The number of informal diamond diggers amounts to 700 000 people [58]. Many of these adults and school-age young people who have left school at a very young age end up working in very difficult and life-threatening conditions. A report issued in 2007 by Jean Baptiste Lubamba provides some pictures of their predicament [60]. In one picture, these workers are shown as reaching and extracting gravel that is 30 to 35 meters below in a shaft or in an underground tunnel. Another picture shows them also seeking diamond in the rivers, “which brings with it the risks of drowning and crocodile attacks” [60].

#### **2.4.5 Income, housing conditions and drinking water issues**

Many households of diamond diggers in Mbuji Mayi “live in hovels, made generally of straw, thatch and mud”. The straw houses, which some rent, usually consist of two rooms. It is here that the entire family of a digger stays. Such a family is generally made up of at least five children. They thus are “living in a state of total promiscuity” [60]. Furthermore, they lack access to quality drinking water, suffer chronic malnutrition, are victims of abject poverty with an income of less than \$1 per day [59,60,61]. The supply of drinking water in Mbuji Mayi is almost nonexistent. Similarly, in the mines, the diggers drink the water from the rivers and streams where they sieve and clean the stones. This water is often the source of illnesses, which sometimes results in deaths. A lot of the diggers’ children do not go to school. From a young age they are recruited into the work of diamond mining, in total contempt of and violation of the rights of children, which are guaranteed by the Constitution of the DRC. The children are also the most badly affected by diseases like malaria or sleeping sickness (7 out of 10 cases) [60].

This socioeconomic context exposes the inhabitants of Mbuji Mayi to suffering from many severe health conditions in addition to HAT as this is explored in this study.

### **3. STUDY PROBLEM AND OBJECTIVES**

#### **3.1 Situation of HAT in eastern Kasai Province**

HAT due to *Trypanosoma brucei gambiense* is endemo-epidemic in Eastern Kasai-province. In 2009, 869 new HAT cases were declared. Since 2010 to nowadays, there is a stagnation of the annual number of new cases of HAT, with an annual average of 533 cases of HAT- infected patients declared [2].

During 2012, a total of 95 cases of HAT infected patients (source population) has been identified and treated at HAT referral and treatment center of Dipumba (RTC) in Mbuji-Mayi. Among these patients, 60 (63.2%) were residents of the city of Mbuji-Mayi. These 60 cases constituted our study sample. The other patients (35 or 36.8 per cent) were transferred from other sites outside of Mbuji Mayi to the Referral and Treatment Center (DIPUMBA) for intake and management [2].

#### **3.2 Study Site Justification and Aims of the Study**

This study is needed at this juncture for at least three major reasons. Firstly, it focuses on the DRC, a country that is most affected by HAT. Secondly, it targets a Congolese province that is ranked as the second worst place in terms of HAT incidence. Thirdly, it looks at a major city at a time where there is not yet a clear understanding of the risk factors that make cities particularly vulnerable to HAT infection. Modalities of transmission and disease expansion in Mbuji Mayi are poorly known. Nobody so far has conducted a study on the social conditions, space occupation and human behavior of HAT patients in that area. In the present study, we want to identify the risk factors of HAT infection in Mbuji-Mayi and we particularly emphasize the socio-demographic characteristics and the human factors that contribute to its transmission. Our aim is to provide a better understanding of the epidemiology of HAT and facilitate the formulation of effective interventions for the prevention of HAT infection in Mbuji Mayi and in other African cities.

## 4. METHODOLOGY

### 4.1 Study Design, Population, and Case-Control Identification

#### 4.1.1 Study design

We used a case-control design as a framework for our research. In this context we provide a clear definition of the population of interest, we delineate the criteria used to select and include some subjects in the group of cases, we specify the matching criteria for the selection of the controls and we describe the procedures used to select the controls.

#### 4.1.2 Population

Under the perspective of our research initiative, we see the overall population of Mbuji Mayi as composed of two categories of individuals. One of the 2 categories includes all the subjects who are HAT-infected and the second category is comprised of all the other individuals who are HAT-free. Due to resources constraints and the overall unknown size of the population of this city, we could neither draw a probabilistic random sample to focus on nor approach each member of these two categories to secure their respective individual data and then explore why those in the first category are sick and why their counterparts in the second category are not. This is the reason why we have used a non-randomized and a non-probabilistic approach. This is why we have investigated few members drawn from these two categories in the context of a case-control design. We have drawn some individuals from the first category (HAT-infected individuals) according to some explicit and logical procedures; and we call these individuals "cases". Similarly we have drawn some individuals from the second category of HAT-free folks to make/label them "controls". We consider that data from these 2 groups of cases and controls will help us get a glimpse of what is really happening in this population in terms of HAT-infection and its risk factors. Below we detail our selection criteria and procedures.

#### 4.1.3 Cases and inclusion/exclusion criteria

We know that HAT-infected individuals have been identified and receive treatment through the center of reference and treatment of the HAT-Dipumba (CRT- DIPUMBA). Based on this knowledge and on information coming from this health care structure, we undertook to select our

cases from the broader universe made of all the individuals who have patronized this health structure in 2012. All HAT patients residing in the city of Mbuji-Mayi, identified and treated at TRC-DIPUMBA in 2012 were eligible. More precisely, the universe was made of all the individuals who meet the following three cumulative criteria: (a) having one's residence in Mbuji Mayi, (b) being of an age equal to or older than 10 years, and (c) having during the period going from January to December 2012 a confirmed pathological diagnosis of HAT. This diagnosis was based not on the results of the card agglutination test for trypanosomiasis (CATT) which is a rapid, simple assay for the detection of specific antibodies in patients with *gambiense* HAT [62], but on the results of the follow-up parasitological tests which are known for their ability to confirm or rule out the presence of the parasites of Trypanosomiasis in some of their specific body fluids. <sup>i</sup>Our thinking is in line with current understanding of the role and usefulness of the various HAT-diagnostic techniques [63].<sup>ii</sup>

<sup>i</sup> CATT is known for its simplicity, reliability and low cost and hence is "used in all control programmes for serological screening of populations at risk for *T. b. gambiense* infection." The test sorts the population between suspect and not suspect subjects. At this juncture the suspected subjects (with positive CATT results) are expected to undergo a battery of other more robust tests which would confirm or rule out the presence of parasites in their systems. It is only when there is evidence of parasites that the person is considered infected with HAT. The CATT-test does not allow diagnosing the disease if it is positive. Nobody can be subjected to the treatment on the basis of a positive CATT-test alone.

<sup>ii</sup> According to the World Health Organization (2014), "serological tests for screening available today are only useful for *T.b. gambiense* infections (Card Agglutination Trypanosomiasis Test or CATT) and establishing suspicion of infection only. Confirmation of infection requires the performance of parasitological tests to demonstrate the presence of trypanosomes in the patient. The parasites can be present in any body fluids. However, the number of parasites can be so low (mainly in the gambiense form of the disease) that available parasitological methods may not be sensitive enough to find them. Thus a negative parasitological result in the presence of a positive serological test does not necessarily indicate absence of infection, and tests may have to be repeated over time to achieve diagnosis." [64,65]

During this period of January to December 2012, 95 HAT patients were registered at the center of reference and treatment of the HAT-Dipumba. Among these individuals, there were 60 residents of Mbuji-Mayi. These individuals were selected and considered "HAT cases." In other words, we have included in the study as cases all the trypanosome-infected patients who have been (a) detected actively during the active campaigns



by the specialized mobile units and passively by fixed health infrastructures, (b) residing in Mbuji Mayi and (c) receiving treatment at the Referral and Treatment Center of Dipumba (RTC-DIPUMBA) in 2012. Only HAT cases aged 10 years or older were considered. The age of the cases varied between 11 and 65 years. This choice was made to ensure that the subjects are able to properly answer the questionnaire. There was no a single case of HAT-infected patient that has reported a change in place of residence.

#### **4.1.4 Controls and inclusion/exclusion criteria**

Each of these 60 HAT cases was then paired with 2 HAT-free subjects (controls). These controls were individuals known to be free of HAT on the basis of a clinical examination and of a negative result following a serological test (Card Agglutination Test for Trypanosomiasis or CATT) [61] in the course of the field survey of May 2014. They were matched using the following three criteria: gender, age and residence in the same local community or “quartier”. Since a case-control design ideally requires assembling a control group comprised of a random sample from the general population that gave rise to the cases [66,67], we used a unique, but logical sampling procedure to ensure that every non HAT infected subject meeting the inclusion criteria had an equal opportunity of being included in the group of controls. This procedure was based on our understanding of the districting of the city of Mbuji Mayi, on our knowledge about the distribution of the HAT cases in the various sub-municipalities of the city and on the availability and accessibility of the basic demographic records at the lowest level of the local communities where people live. Indeed, from an administrative perspective, Mbuji Mayi is subdivided into five sub-municipalities or “communes” (Commune of Bipemba, Commune of Dibindi, Commune of Diulu, Commune of Kanshi and Commune of Muya) that are in turn subdivided into local communities or “quartiers.” The total number of local communities in Mbuji Mayi is 157.<sup>iii</sup>

<sup>iii</sup> *Thirty-six (36) of these local communities are parts of the Commune of Bipemba which sub-municipality was known to have eighteen (18) HAT cases; thirty-eight (38) of these local communities are parts of the commune of Dibindi which sub-municipality was known to have 20 (twenty) HAT cases; thirty-two (32) of these local communities are parts of the commune of Diulu which sub-municipality was known to have six (6) HAT cases; eighteen (18) of these local communities are parts of the commune of Kanshi which sub-municipality was known to have five (5) HAT cases; and thirty-three (33) of these local communities are*

*parts of the commune of Muya, which sub-municipality was known to have eleven (11) HAT cases. Knowing that these 60 cases resided only in some of the 157 local communities which are integrating parts of the five sub-municipalities (or “communes”) that make up the city of Mbuji Mayi, we went only to these specific local communities known to have HAT cases and here we enlisted the support of the local authorities who all were kind enough to provide our team with the register of all their local residents.*

Knowing that these 60 cases resided only in some of the 157 local communities which are integrating parts of the five sub-municipalities (or “communes”) that make up the city of Mbuji Mayi, we went only to these specific local communities known to have HAT cases and here we enlisted the support of the local authorities who all were kind enough to provide our team with the register of all their local residents. For each of the cases, we implemented the following procedure to select two controls that were to be residents in the same local community and to be of the same gender and age group like the case. For instance, for one female HAT case of 18 years in a given local community or “quartier” in the Commune of Bipemba, we pulled from the local register all the names of 18-20 years female residents and then we randomly selected two individuals and two additional reservists from this list. We then visited and asked these 2 main individuals to participate in the study. Following their consent, these individuals were tested with the CATT-test to ascertain their negative status. If any of them were positive, they were excluded; and in this case, a reservist was approached, recruited, tested, and eventually surveyed/questioned. In each target local community a neutral child was asked to blindly pull the two names of the controls and of the reservists from a box in which the names of all the potential controls of the same local community were included. This process had the disadvantage of excluding the potential controls from some of the local communities that did not have positive HAT cases known at the Referral and Treatment Center of Dipumba, but it gave an equal chance to all the potential controls within the target local communities that had positive HAT cases. We did neither purposely seek to select controls that were neighbors of the HAT cases nor to achieve complete matching on all the features of residence. Hence, the controls were not expected to have in their places of residence all the features found where the cases resided. Being only co-residents in the same local communities with the HAT cases, the controls could possibly have in the proximity of their residences some features that were

dissimilar to those in the specific places where the corresponding cases lived such as hog farming, albeit in the same local communities. In other words, there was commonality of living in the same local communities, but not necessarily proximity of neither housing nor sharing of all the other features in the living space. This situation could explain why some factors related to housing could differ between cases and controls. This matching process served to control for the possible confounding effect of these 3 factors, and thereby served to maximize the analytical power of the study. The age of the controls varied between 11 and 65 years. This choice was made to ensure that the subjects are able to properly answer the questionnaire. In the recruitment of controls, we excluded any of the aforementioned subjects as well as any persons who lived together with the cases.

## 4.2 Data Collection

This survey was approved by the local authorities and the provincial ethics committee. The cases and the controls were informed of the purpose and expectations of the study; they have all provided a proper verbal consent (adults) or proper assent (for minors) to be participants in the study. These 60 HAT patients (cases) and the 120 healthy subjects (controls) have responded to a structured questionnaire. The questionnaire had been previously pretested on 20 sick HAT patients who were under treatment in 2013 and on 40 controls, and it was then refined before the start of the survey in May 2014. The study questionnaire was designed in French and the data collection technicians were instructed to use French as this is the official language of the DRC. However, to successfully obtain data from some subjects who, by virtue of their low school attainment, do not have a good command of French, the data collection technicians were instructed to use Tshiluba, one of the four national languages of the DRC in which most people in the Eastern Kasai province are fluent. For each case and each control, we collected general demographic characteristics as well as data on beliefs, knowledge, practices and activities considered as potential enabling and risk factors for HAT. The interviews were held at their respective homes. In consideration of the fact that our study only involved minimal risks for the subjects, we instructed our data collection technicians to comply with the following guidelines when they approach adult and minor subjects. *Procedure of Data Collection from Adult Subjects:* If the study subject was an adult, the

data collection technician informed him/her about the nature and objectives of the study and then asked the subject if he/she was willing to be participant. The data collection technician made a note of the given verbal consent on the questionnaire used for each subject. *Procedure of Data Collection from Minors:* If the subject was a minor (less than 18 years), the data collection technician first talked to and requested the permission of any available parent or legal guardian of the minor. Subsequent to securing that permission, the technician explained the nature and objectives of the study to the minor and then asked the minor to provide his/her verbal assent (as typically, children do not have the legal capacity to consent to participate in research). The data collection technician made a note of the given assent on the questionnaire used for each minor who participated in the study. The children were involved in the process as they were able to assent (i.e., capable of having a study explained to them and/or reading a simple form about it, and giving verbal or written agreement if they decide to participate in the study). A copy of the survey questionnaire is available and can be provided on request. Besides primary data collected through the survey of cases and controls, additional data have been extracted from the annual reports of activities of the Referral and Treatment Center of DIPUMBA.

## 4.3 Data Processing and Analysis

The data has been entered on a spreadsheet before its analysis using STATA, a statistical analysis software (version IC 12.0). The association between the different factors studied and HAT infection has been determined by estimating the odds-ratio (OR) with a confidence interval (CI) of 95% and a p-value of less than .05. This has been achieved by using the univariate and multivariate methods of logistic regression analyses.

## 5. RESULTS

### 5.1 General Characteristics of Cases and Controls

Pertinent features of the study and control groups are compared in Table 1. The study involved a total of 180 subjects (60 cases and 120 controls) who were interviewed. The 60 cases were predominantly male (male-female ratio of 2.2:1) with the majority (53%) in the age group of 20-40 years. The next age group in

terms of percentage is 40 years and older with 28.3% of the subjects in this group. The same pattern is seen on the control group. In accordance with the design of the study, the male-female ratio and the distribution of the subjects according to age corresponded closely to those of the controls. The age of interviewees varies from 11 to 65 years. The average age of the HAT cases was 33.5 years (SD = 12.8 years). Among the cases, subjects in the most economically productive age group (20-40 years) were the most affected.

The HAT cases were found throughout the entire city; that is, in all the 5 municipalities of the city: 20 cases in the commune of Dibindi, 18 in Bipemba, 11 in Muya, 6 in Diulu and 5 in Kanshi. The average household size is 7.1 persons (SD = 2.8 persons). The survey data showed that 78.3% of the cases and 82.5% of the controls belonged to households of very large size exceeding 5 persons ( $p > .05$ ). In HAT patients, those born in Mbuji-Mayi represent the majority (66.7%). This proportion is 75% among the controls. Among the respondents, 33.3% of the cases are migrants, that is to say persons born elsewhere who then have settled in Mbuji-Mayi. The analysis of the religious affiliation leads to the finding of a city heavily christianized with 91.7% of Christians against 8.3% of the Muslims. Catholic and Protestant affiliations represent respectively 25% and 15% for cases vs 27.5% and 16.7% for the controls. Among the 60 HAT patients, 19 (31.7%) compared to 49 (35%) controls had a low level of education (non-schooling and primary school level), 68.3% of the HAT cases have achieved the level of secondary school. The main activities (agriculture, livestock, trade in rural areas and diggers of diamond in the mines) in which the majority of HAT cases (45%) are involved are risk prone activities. The practice of secondary activities to supplement one's income is very frequent in Mbuji-Mayi. Trade in rural areas and diamond digging activity remain the largest secondary activities practiced by the cases (63.3% and 51.7% vs 46.5% and 33.3%;  $p = .034$  and  $p = .018$ ). The majority of cases 44 (73.3%) and controls 95 (79.2%) have already heard of the existence of the HAT in Mbuji-Mayi.

Among the 60 HAT patients, 58 subjects (or 96.7%) were known to be at the meningitis-encephalitic or neurological stage (stage 2). Two patients (or 3.3%) were at the hemo-lymphatic stage (stage 1). Five HAT patients (8.4%) were detected in a passive way by the fixed health

facilities (hospitals, health centers), 55 patients (91.6%) have been diagnosed by the specialized services for HAT elimination. Among the 55 HAT cases, 44 (73.3%) patients were diagnosed in a passive way by health structures that are specialized for HAT diagnosis, treatment and control and 11 (18.3%) patients were diagnosed in an active way by specialized HAT mobile units.

In regard to activities connected with water supply for household needs, HAT positive subjects reported drawing water from wells (16.7% vs 6.7%;  $P > .05$ ), walking along the river bed and in the peat lands (11.7% vs 9.2%;  $P > .05$ ). The HAT cases reported involvement in various activities that put them in much closer proximity with the watercourses: bathing (8.3% vs 6.6%;  $P > .05$ ), engaging in dish and laundry washing (20% vs 37.5%), fetching household water from rivers (50% vs 24.2%;  $P < .0001$ ), cassava retting roots (1.7% vs 7.5%), digging diamond in the mines (51.7% vs 21.6%;  $P < .0001$ ), trafficking or buying diamond from mine diggers (13.3% vs 8.3%;  $P > .05$ ).

The data on dwelling space have been collected. The environment of the habitat, especially its proximity to risky sites for contact between humans and tsetse flies has been examined. More than half of the cases (55.1%) and more than half of the witnesses (68.4%) resided close to wells, diamond mines, water streams and marshy areas, 45% against 31.6% of the controls in the vicinity of the savannahs, pig farming (existence of a herd in the neighborhood) and various plantations.

The data on the types of toilet used show that defecation in the open (in the surrounding undergrowth, near or in a river or creek) is still the type of toilet used by a non-negligible proportion of the cases (10% vs 5.8%;  $P > .05$ ). The proportion of people who know HAT and the tsetse fly as a vector of this disease is relatively high (86.7% of cases vs 77.5% of the controls) in both groups. The mode of HAT transmission was mentioned by 75% of the cases and 53.3% of the controls (bite by infected/contaminated tsetse). The path of blood transfusion and the vertical transmission (from mother to child during pregnancy/before birth) have not been mentioned. Some modes of erroneous transmissions have been cited such as physical contact with HAT patients.

The manifestations of HAT that are most known by the cases are, in descending order of

importance, sleep disorders (daytime sleepiness and insomnia night) cited by less than half of the cases (31.7%) and controls (40.8%); slimming (30% vs 22.5 %) and mental disorders (23.3% vs 17.5%). No one either among HAT cases or among their controls has cited cervical adenopathy. The majority of HAT cases are aware that HAT reaches the entire world (71.7% vs 68.3%); they also know that the HAT is curable (83.3% vs 72.5%). Less than half of the controls (48.3%) are not afraid of a close contact (eating and sleeping together) with HAT patients. A non-negligible proportion of the cases (23.3%) and controls (28.3%) believe in the mystical origin of the HAT (witchcraft).

The majority of cases (76.7% vs 54.2%;  $p = .03$ ) are favorable to HAT screening. A low proportion of cases (33.3% vs 25%) have cited the fixed health structures as a place recommended for HAT screening.

Concerning the health care facilities, the majority of HAT patients (83.3% vs 55%;  $P = .004$ ) was aware of and cited the specialized centers of fight, treatment and control of HAT. Less than half of the cases (41.7%) were aware that prevention of the HAT is possible. Barely 32% of the cases and 36% of the controls mentioned the trap to tsetse flies as a mean of primary prevention of HAT.

## 5.2 Risk Factors

The results of the univariate logistic regression analysis (non-adjusted OR) show the factors significantly associated with HAT infection in Mbuji-Mayi. Based on the computed odds ratio (OR), the following factors emerge as having a significant influence on HAT infection:

**Table 1. General characteristics of cases and controls in the 2012 survey on risks factors of human African Trypanosomiasis (HAT)**

Characteristics and modalities	HAT cases (n = 60)	Control group (n = 120)
<b>Sex</b>		
Female	19 (31,7%)	38 (31,7%)
Male	41 (68,3%)	82 (68,3%)
<b>Age group</b>		
>20 years	11 (18,3%)	17 (14,2%)
20-40 years	32 (53,4%)	59 (49,1%)
<40 years	17 (28,3%)	44 (36,6%)
<b>Disease stage</b>		
Hemolympathic stage	2 (3,3%)	NA
Meningo-encephalitic stage	58 (96,7%)	NA
<b>Screening mode</b>		
Active	11 (18,3%)	NA
Passive	49 (81,7%)	NA
<b>Professional activities<sup>1</sup></b>		
Farming	16 (26,6%)	33 (27,5%)
Trading in rural areas	38 (63,3%)	56 (46,7%)
Diamond diggers	31 (51,7%)	40 (33,3%)
<b>Water-related activities</b>		
Dish/Cloth washing	12 (20%)	45 (37,5%)
Household water fetching	30 (50%)	29 (24,2%)
Mine Diggers	31 (51,7%)	26 (21,7%)
<b>Proximity of housing</b>		
Diamond mining	10 (16,7%)	17 (14,2%)
Swamps and plantation fields	10 (16,7%)	15 (12,5%)
Savannahs	24 (40%)	31 (25,8%)
Rivers/creeks/Water streams	16 (26,7%)	57 (60,8%)
<b>Knowledge of transmission modality</b>		
Tsetse bite	45 (75%)	64 (53,3%)

<sup>1</sup> = The percentages exceed 100% because some individuals have reported performing two or three of these groups of activities

The activity of fetching water from the river to satisfy household needs increased the risk of contracting HAT by a factor of 1.9 (OR = 1.9; 95%CI: 1.5 -2.6; P< .0001).

The activities in relation with or in close proximity with watercourses are significantly associated with HAT infection: diamond digging in the mines (OR 3.86 ; 95%CI: 1.98 - 7.53; p<.0001); fetching water from the river (OR = 3.13; 95%CI: 1.62 - 6.04; P = .001) ; dish and cloth washing (OR = 1.4; 95 %CI: 1.1 - 1.8; P <.004); retting fresh cassava roots to the river (OR = 3.1; 95 %CI: 2.1 - 4.9; P < .0001); travel for trade in rural areas (OR = 1.97; 95%CI: 1.04 - 3.72; P = .036); the existence of hog farms in one's entourage (OR = 2.3; 95%CI: 1.7 -3.1; P < .0001) and the proximity of the habitat with the savannas (OR = 2.4 ; 95%CI: 1.7 -3.3; P< .0001).

Using the logistic regression multivariate analysis, we got the following results (also displayed in Table 2): The supply of water to household and activities carried out in close proximity with a river multiplied by 3.5 the risk of HAT (Adjusted OR = 3.5; 95%CI: 1.2 -10.7, P = .05). The activity of digging diamond multiplied by 4.13 (Adjusted OR = 4.13; 95 %CI: 1.89-9.00; P < .0001) the risk of HAT. The proximity of a hog farm multiplied by a factor of 2.6 the risk of acquiring HAT (Adjusted OR = 2.6; 95 %CI: 1.3 - 5.2, P = .01). Dish and cloth washing in the water stream multiplied the risk of acquiring HAT by a factor of 1.7 (Adjusted OR = 1.7; 95 %CI, 1.1 - 2.6, P = .05). Engaging in trade activities that involve travelling to rural areas multiplied the risk of acquiring HAT by a factor of 2.32 (Adjusted OR =2.32; 95 %CI: 1.07 - 5.02, P = .032).

## 6. DISCUSSION

In the DRC, research studies regarding the risk factors of the HAT have been very limited and rarely found in medical literature. A group of researchers conducted a case-control study in Kinshasa, capital of the DRC, in an endemic area

of *Trypanosoma brucei gambiense* [31]. As this was the case in the aforementioned study, the present study shows that some groups, some activities and some environments increase the risk of acquiring HAT. HAT equally infects men and women. We found that among the diagnosed and treated HAT cases, there was 68.3% of men and 31.7% of women and this difference was not significant (p> 0.05). These results corroborate previous findings [17,19,26] [29,68] which indicated that sleeping sickness reaches people of both genders.

HAT does equally infect subjects of all age groups. The majority of subjects infected with AT are aged from 20 to 40 years, an age group known as made of those who are professionally and economically active. This finding has already been reported by several authors who indicated that the active persons are the most affected [17,31,32].

Active screening provided by the specialized mobile units regarded as effective means to identify the maximum number of HAT cases had contributed in 18.3% of the cases to the detection of new cases during the period of our study. Passive screening provided by the fixed health structures working independently from the national program of fight against HAT (PNLTHA) contributed only for 8.4%. The majority of HAT cases (73.3%) have thus been passively identified by health structures that are specialized for HAT diagnosis.

Most of the HAT cases (58/60 or 96.7%) were in meningo-encephalitic stage (stage 2). This means at an advanced stage of the infection. The ratio stage 2 on stage 1 was 29 in favor of stage 2. This ratio is 7.4 times higher than that found in Kinshasa [29]. Our results confirm findings of Miaka et al. [19] which indicated that the passive screening performed by the non-personal forms to the diagnosis of HAT, represented only 37 cases (2.75%) of 1345 cases detected in two years (1998-1999).

**Table 2. Determining factors of HAT infection in Mbuji Mayi**

Determining factors	Adjusted odd ratio	95% Confidence interval (CI)	p-value
Fetching water for household needs	3.5	1.2 – 10.7	.05
Diamond Digging	4.13	1.89 – 9.00	.001
Closeness of Hog Farms	2,6	1,3 – 5,2	.01
Dish and Cloth Washing	1,7	1,1 – 2,6	.05
Trading in rural areas	2,32	1,07 – 5,02	.032

These results corroborate the data described elsewhere according to which active screening is no longer more efficient in urban areas [19,69,70,71]. This observation also confirms the results of previous work conducted in the DRC [19,27,71] and elsewhere [69,72,73], according to which, screening in an urban environment has not the same effectiveness as that achieved in rural areas. As has been noted in other studies [36,70,74], the negative organizational features such as weak logistical means and shortage of specialized mobile teams could explain this lack of effectiveness of the active campaigns in urban areas. The Eastern Kasai province has only four specialized HAT screening mobile teams. Mpanya [75] mentioned that the stagnation of HAT prevalence in the provinces of Bandundu and Kasai is explained by the low rate of participation of the exposed population to the active screening program.

The city of Mbuji-Mayi is experiencing a very severe drinking water shortage. The study shows that the HAT cases are involved at a greater rate into activities involving presence of or proximity of water streams, particularly those activities aimed at fetching and supplying water to their households. These HAT cases also practice certain activities in relation with water streams such as dish or cloth washing and digging diamond in the mines. One 1993 study in the Ivory Coast shows that the use of a water point for natural/collective needs (wells, river etc.) by a group creates a high risk of acquiring sleeping sickness [76].

Most of the HAT cases resided near savannah (40%), water wells (20%), diamond mines (16.7%) and marshy areas (11.7%). Other studies mention that the proximity of the habitat with some areas such as hog farms and wells constituting a favorable biotope/conducive to the multiplication of vectors could be a risk factor [39,77].

Through the univariate logistic analysis, diamond diggers constitute the group at high risk of HAT infection. This observation corroborates the results of previous work [35,75,77] according to which, the socio-economic and cultural contexts of the population at risk in the two provinces, Bandundu and the Eastern Kasai are different. In the province of Bandundu, the at-risk population lives in the savannah mainly on agriculture. By contrast, in the Eastern Kasai, the-at-risk population lives in the diamond mining camps and along water streams. More precisely, in endemic and tsetse infested areas, water supply

at the various natural access points significantly increases the risk of HAT infection. According to Meda et al. [76], the vector of HAT (*Glossina palpalis flies*) is particularly abundant near the water points frequented by the human beings from which it gets its food.

The data on the dwelling space show that the subjects residing close to Savannah are more exposed to the disease, probably because of the less number of animals found in that area. The presence of pigs around the habitat (which can be either a barrier or an attraction) appears in our study area as a risk factor for acquiring the disease. In fact, Meda and his colleagues [76] mentioned that the presence of pigs around the habitat plays two contradictory roles, a protective role by way of diverting the tsetse flies from the human bait and a role of potential reservoir of the zymodemes which have been isolated in this animal in the Ivory Coast and which are infectious for humans.

The analysis using a logistic multivariate regression model shows that the risk of infection increases in response to digging diamond in the mines. More clearly, HAT cases engage much more in this type of activity than their controls (Adjusted OR = 4.13). So far no study has been conducted in Mbuji-Mayi or on this at risk group, a situation one is less likely to encounter in urban areas, and especially not in the world capital of diamond. This investigation linked the activity of fetching water or engaging in other activities in close proximity with water sources as a risk factor of HAT. It has pinpointed the negative role that fetching water in natural collective sources (wells, water course) is playing in the transmission chain. At these places where they daily come unsuspecting of anything, the healthy individuals come across infected tsetse flies; at these places where infected tsetse flies roam, unsuspecting healthy individuals connect with the vector of HAT as they engage unsuspectingly in dish and cloth washing. Moreover proximity of a hog farms and trading in peripheral urban and urban settings increase the risk of acquisition of the HAT. Similar findings have been reported by other authors [61,63,76]. This observation corroborates the data of various entomological investigations, which located the biotopes favorable to tsetse flies along the course of water [69,77,78]. Further studies need to be carried out in Mbuji-Mayi in order to identify transmission sites and define transmission cycle of the disease.

## 7. CONCLUSION

The results of this study reflect the reality of the current importance of HAT in Mbuji-Mayi. The study has identified a higher risk of transmission linked to the activity of artisanal diamond digging, to the water source related activities, to the localization of human residences in savannah, to the presence of hog farms in the midst of human agglomerations and to the involvement in trade in peripheral and rural areas. It has pointed out disconcerting delays in the detection of cases. It has highlighted the importance of integrating effective mass screening in the fixed health structures. When it is adopted, such integration will be accompanied by the information and the education of the populations as well as the training of health personnel in Mbuji-Mayi who are not seasoned to the principles and practices of HAT screening and elimination. A specific program of active screening at diamond mining camps along with the establishment of a sustainable and permanent system for safe water supply can significantly reduce the incidence of HAT in Mbuji-Mayi. The most enduring solution to the HAT plight necessarily calls for a comprehensive community development plan and an improvement in the living conditions and the well-being of the population.

Although this study has only dealt with 180 subjects and although its results cannot be generalized to the whole population of Mbuji-Mayi, it does provide a glimpse of the reality facing the population of a Congolese city in the context of a country under a chronic political instability. There is a definite need to launch extensive epidemiological studies in which a much larger number of HAT cases would be involved. Such extensive studies will have the greater advantage of leading to more robust findings to instruct HAT program development and implementation.

## CONSENT

All authors declare that verbal informed consent was obtained from the patients and the controls. For any minor subjects, consent was asked and obtained from an adult parent.

## ETHICAL APPROVAL

All authors hereby declare that all interviews have been performed in accordance with the

ethical standards laid down in the 1964 Declaration of Helsinki.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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