T.R.N.C

NEAR EAST UNIVERSITY INSTITUTE OF HEALTH SCIENCES

COMPARATIVE STUDY OF STRATEGIC APPROACHES TO THE SCREENING AND DIAGNOSIS OF HUMAN AFRICAN TRYPANOSOMIASIS IN THE FIRST STAGE FROM 2015-2017 IN THE CITY OF BANDUNDU IN DEMOCRATIC REPUBLIC OF THE CONGO.

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DEDICATION

I dedicate this work

To my mother Vitalie MAMFIEMA,

To you a my elder brother, Gaspard KILA

To you my wife Sarah BIRI-BIRI IZENE

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To Assistant Professor Dr. Özgür Tosun, Departement of Biostatistics, and Faculty of Medicine at Near East University in North Cyprus; who did us honor to accept the direction of this thesis and to judge our work; that he finds here the testimony of our deep respect and admiration for his knowledge and the passion that animates him.

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Daniel Kitima Nkila

ABSTRACT

COMPARATIVE STUDY OF STRATEGIC APPROACHES TO THE SCREENING AND DIAGNOSIS OF HUMANAFRICAN TRYPANOSOMIASIS IN THE FIRST STAGE FROM 2015-2017 IN THE CITY OF BANDUNDU IN DEMOCRATIC REPUBLIC OF THE CONGO.

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Human African trypanosomiasis is a major public health problem in sub-Saharan Africa, including the Democratic Republic of Congo, which is currently considered the epicenter of this parasite in Central Africa. (36 million people exposed 64%). The subject of our study is a comparative study of strategic approaches for screening and diagnosis of HAT in the first stage of 2015 to 2017, in the city of Bandundu in DR Congo.

This study was done in the provincial coordination of the national program against THA / Kwilu North, whose data collection from 2015 to 2017,267 patients were screened and diagnosed with HAT. The descriptive statistics show that 63.30% are female while 36.70% are male. About 43.80% of the cases are passively screened while 56.20% of the cases are actively screened.

Using the Chi-Square Statistical Test at a significance level of 0.05, the result shows that being a male or a female does have a statistically significant effect on what stage they could be when screened. Also, it was found that the type of village of the participants tends to influence the types of the Screening method adopted. The outcome of passive screening (population coming to designated test centres) method is found to be more effective in suburbs environment while active screening, which involve mobile health team workers to go an outreach is found to be more effective in the hinterlands and villages

Keywords: Screening, Parasite, Diagnosis, Trypanosomiasis, Epidemiology

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LIST OF ABBREVIATIONS

HAT	Human African Trypanosomiasis
WHO	World Health Organization
DRC	Democratic Republic of Congo
CSF	Cerebra Spino Fluid
PNLTH	National Program for the Control of HAT
DNA	Deoxyribonucleic acid
DFMO	Difluoro-methyl-ornithine
DA	Active Screening
DP	Passive Screening
CATT	Card Agglutination test for Trypanosomiasis
INRB	National Institute of Biomedical Research
CTC	Centrifugation in Capillary Tube or (woo Test)
GE	Thick drop
NECT	Nifurtomox Eflornithine Combination Therapy
LAV	Anti-Vector Fight
PG	Ganglionary Puncture
CDTC	Diagnosis center Treatment and Control of HAT
MEACT	Mini Anion Exchange Centrifugation Technique
PCR	Polymerase Chain Reaction
NC	New Cases
	WHODRCCSFPNLTHDNADFMODADPCATTINRBCTCGENECTLAVPGCDTCMEACTNEACT

20 AC Old Cases

- 21 CNS Central nervous System
- 22 QBC Buffy Coat Technique
- 23 NASBA Amplification nucleic acid sequences
- 24 ELISA Enzyme Linked Immuno assay
- 25 TI Infection Rate

CHAPTER ONE

1.1. Introduction

According to Hana Talabani et al. (2011), Human African Trypanosomiasis, or sleeping sickness, is defined as a parasitic disease caused by trypanosoma bruceigambiense and transmitted to humans by the bite of tsetse flies. This disease is exclusivelyon the African continent, between 15 °of latitude north and 20 ° of southern latitude.

Globally, the number of reported cases found outside Africa does not exceed fifty per year(Lejon et al., 2003). Another form of sleeping sickness is in America calledAmerican Human Trypanosomiasis or Chagas Disease. It is endemic in Latin America. One study, in 2006, 3.5% of cases were found to immigrants from Latin America to Canada. 5% to 10% of newborns to mothers infected with the disease were also reported. In the United States, 30 cases have been reported in the last century (Noni MacDonald, 2014).

In Europe, the largest number of cases reported contains 109 cases observed between1904 and 1963. The incidence of imported sleeping sickness is very low because of avery limited distribution of the disease in patients. Tourists who often spend holidays inAfrica, in endemic areas. This can increase the incidence of this disease. In France, bioclimatic conditions do not provide a suitable habitat for the installation of vectors, accidental transmission in the laboratory has been reported. A survey covering the period 1980-2004 reported 26 published cases (Legros et al., 2006). It is thus a pathology observed exceptionally in France and the diagnosis can be evoked only if there exist the notion of stay in the endemic zone of the HAT.

There are two forms of HAT, namely T. b. Gambiense, endemic in West and Central Africa and account for 97% of cases; it has a chronic evolution and T. b. Rhodésiense form or rh, endemic in Eastern andSouthern Africa, with 3%.

Clinically, the disease has two phases, namely: the first phase during which the parasites are present in the lymphatic, blood system and the second phase if they have entered the brain. In the 1960s, HAT was fiercely combated, but by the beginning of the 21st century, there were an alarming number of new cases, with approximately 300,000 people infected, as a result of decades of neglect, leaders of African countries, after the departure of colonial governments. This reappearance of this disease was considered a public health disaster. The population at risk of HAT infection in Africa has been estimated at 57 million. The World Health Organization (WHO) responded by taking a number of initiatives to reverse this situation. Although these measures, the fight against HAT, was not well conducted as in the colonial period.

It mainly concerns a poor person living in rural areas where there are few health structures, which makes it difficult to diagnose the disease in time.

According to the World Health Organization (WHO, 1994), Trypanosoma brucei gambiense is found in 24 countries in West and Central Africa. Another form is Trypanosoma Brucei. (Aubry Pierre 2017) indicates that in 1998, nearly 40 000 cases were reported, including 300 000 undiagnosed and therefore untreated. According to Eric

Ismael Zoungrana (2009), the trypanosome can always become virulent: the mortality is 100% in the absence of treatment and good care. In the continuity of its affirmation, it is more than any other country effective in the surveillance of populations at risk: early detection by mobile teams and systematic treatment of patients and reduction of populations: vector control. The actual number of cases is 20,000. Seventeen countries in sub-Saharan Africa reported cases of HAT to WHO in 2009. Seven out of seventeen countries accounted for 97% of reported cases, in Angola; Uganda, South Sudan, Central African Republic, Congo, Chad and Democratic (DRC). The geographical distribution of HAT is directly related to that of its vector, the tsetse fly. It is located in intertropical Africa between latitudes 14 $^{\circ}$ north and 29 $^{\circ}$ south; HAT outbreaks do not cover the entire area of distribution; their limits depend on the existence of epidemiological conditions favorable to the appearance or maintenance of the disease. Thus, in the savannah, this depends on the behavior of anthropophilic flies; the disease is superimposed on the network of forest galleries while its distribution is much more diffuse in the forest (Brun R et al., 2010).

In Uganda, there are both types and some patients may be co-infected with Trypanosoma brucei gambiense and Trypanosoma brucei rhodesiense (Kennedy PGE, 2010).

The DRC is one of the largest countries in sub-Saharan Africa. It is about 33 times larger than the Benelux and four times larger than France, eighty times larger than Belgium. It has an estimated population of 89,762,749 inhabitants in 2017. An area of 2,345,410 km², slightly less than a quarter of that of the United States. Its density is 38.27 inhabitants / km².

Human African Trypanosomiasis can take epidemic form in DRC, It is observed the hight rate of mortality, and it is significant especially in rural area.HAT which causes a chronic form of the disease.

Nevertheless, with the efforts undertaken by the Ministry of Health through its specialized program, the National Program for the Control of HAT, this last decade has seen a significant decrease of the cases number reported of sleeping sickness throughout the world.Indeed, this number increased from 26.000 cases in 1996 to less than 2500 cases compared to 2015. This drastic decrease should not, however, lead to an abandonment of the fight before reaching the critical threshold of elimination if no interruption of transmission throughout the Republic. During the colonial period, thanks to a political of struggle based on active research, the correct case management and carried out with adequate means, the HAT was fiercely combated, to achieve on the eve of independence a rate of very low infection, less than 1 case per 10000 inhabitants (Mukengeshayi, 2016).

In DRC, the population at risk is from (36.2 million), or 64%, is really a major health problem. The DRC alone accounts for 74% of cases. It is still in the lead in case notification.

1.2. Objectives of the study

This studyhas asobjective toidentify best approach to screenearly, in the currentepidemiological context in (DRC) with the North Bandundu coordination structures that have incorporated strategies for the control of HAT.

The study will also help identify screening method most suitable for the identification persons suspected of being infected with Trypanosomiasis since in the DRC, twostrategic approaches are used at the level of fixed health structures responsible forscreening for sleeping sickness, either by mobile teams or stationed healthcare testingcentres. The first approach is Active Screening (AS) which consists of an active searchfor suspects by a complete examination of the entire population in a well-defined administrative entity (villages or neighborhoods in a city or city) endemic while thesecond approach or passive screening (PS), is based on the fixed health structures and hospitals, Center of diagnosis, treatment and control (CDTC).

1.3. Significance of the Study

The importance of this study, help to have better diagnostic approaches to HAT, facilitating the screening of all suspects of the said disease, with a view to reducing morbidity and mortality in the health zones. The study will also offer insight to Congolese health care institutions on how to reduce the risk of the disease, especially location wise improvement of population population to this endemic. It also contributes to deepening our knowledge of HAT control measures, so it can serve as a milestone for future research in the country.

1.4. Thesis Structure

The Chapter one of the studies began with an introductory background of Trypanosomiasis in Africa and in a global context. Also, the objective of the study and its significance was discussed. The Chapter two provided the literature review and concepts of the study. Here, further discussion of the epidemiology on HAT was given. Also, the discussion of the HAT relative to the biological and clinical operating and transmission cycle was discussed. The Chapter three explained the research methodology adopted as well as the overview of the data utilized. The Chapter four presented the result of the data analysis as well as the discussions. In Chapter five, a summary of the findings was given and suggestions on how various stakeholders in the research of HAT can better contend against this epidemic in DRC. Also recommendations for future research activities were provided.

CHAPTER TWO

GENERAL INFORMATION

2.1. Definition of Basic Concepts

Study: According to Larousse (2018), the study is an intellectual effort oriented towards the observation and understanding of beings, things, events. It is also an intellectual effort directed towards the acquisition of knowledge towards the learning of something. For this work, the study is considered as the methodical application of the mind seeking to understand and learn strategic approaches to the diagnosis of early HAT.

Comparative: Larousse (2017), considered it as the degree of comparison of the adjective or the adverb expressing a quality to a higher or lower degree in respect to another. Or at the same qualityconsidered in respect to another. Thus the comparative study is considered as intellectual operation to compare the results of the passive and active approach to the diagnosis of HATin the first stage.

Strategic Approaches

- **Approach**: The approach is the highlighting of a set of related methods of determining disciplines that can quickly and effectively solve the biggest problem in society (Tez, 1968).
- **Strategy**: The term strategy refers to a set of coordinated, implicit or explicit actions, operations, ruses, skillful maneuvers and allocation of resources, in order

to achieve global and fundamental objectives in the long term. (Jean-Claude Besson-Girard, 2005). It is the science of coordination, planning, implementation, evaluation and monitoring of activities related to the fight against HAT.

Strategic Approach: It is the highlighting of a set of attached methods of determining disciplines to coordinate, plan, execute, evaluate and monitor activities related to the fight against HAT.

Diagnostic: The diagnosis includes all the tests performed by a health professional to understand the pathology of a patient. The diagnosis is based on a clinical examination, a precise questionnaire that allows the patient to discuss his symptoms, radiological or laboratory examinations. The clinical examination usually includes palpations, measurements of blood pressure or heart rate, an inspection, control of reflexes. Listening to the patient is of great importance in the diagnosis (Jeff, 2008).

For this study, the diagnosis is considered as the screening or the identification of persons suspected of HAT. In the framework of this study, we have two types of diagnosis or screenings, which are practiced in the fight against HAT, namely Passive and Active Screening.

Passive Screening: To detect suspicious cases that arrive at the fixed health services (Health Centers, Hospitals and CDTC) and examination for confirmation of the diagnosis of HAT, this mode of screening that takes place in health centers is called passive screening. It is the most practiced and ensures the sustainability and quality of diagnostic activities in HAT control programs. This screening method must be supported by a community awareness and information campaign

about the signs of the onset of HAT and the availability of free and effective treatment.

) Active screening: Suspected cases of HAT are grouped together and examined for the diagnosis of HAT in villages and neighborhoods or towns / cities outside health services, when health workers are moved to the locality. This is a commonly known approach. An advanced strategy is recommended in more endemic villages and social mobilization is the first step in this strategy. It is carried out by the mobile team specialized in HAT, which must carry out its monthly visits according to its reprogramming. (Knut Lönnroth and al, 2013).

HAT: According to Eric Ismael ZOUNGRANA (2009), Human African Trypanosomiasis (HAT) is a protozoan,trypanosome, transmitted by flies or tsetse fly).

Moreover, HAT is considered according to Hana Taliban et al., (2011), as a parasitic disease occurring exclusively on the African continent between latitude15° North and 20° south. Its common denomination of "sleeping sickness" often makes us forget its extreme gravity, characterized by a meningoencephalitis of constant fatal evolution in the absence of treatment. It caused by Trypanosoma brucei gambiense and transmitted to humans by bites of the tsetse fly in West and Central Africa.

First Stage: The first stage is the beginning phase of any disease. In this study, it is the period of manifestation of the first signs of the HAT, these signs are: chronic and intermittent fever, headache, pruritus, lymphadenopathy, weakness, asthenia, and anemia and, in to a lesser extent, hepatosplenomegaly

Second Stage, The second phase succeeds to the first, it manifests itself by themeningoencephalitic, begins when trypanosomes invade the central nervous system (CNS). Neurological signs and symptoms, including sleep disturbances, are characteristic of the second stage.

2.2. Theorical approaches to African human Trypanosomiasis

2.2.1. History of HAT

Sleeping sickness is probably as old as mankind, but it is first reported in 1374, when the Sultan of Mali died after a long illness ending in a state of continuous sleep. The slave traders already understand the consequences of this disease: all slaves with large ganglia at the base of the neck are removed. They must wait another 350 years (1724) for the first description of the disease to be made. But the parasite responsible for the disease is identified. For his part, Forde (1901) sees "mobile vermicles" in the blood of a boat captain who has been fluvial for six years in The Gambia. Dutton (1902) examines the patient's blood and identifies a Trypanosome he described as Trypanosoma gambiense.

In 1903, in the Gambia, the presence of Trypanosomes in human blood is confirmed: everyone thinks that this parasite is very pathogenic and has no relation with sleeping sickness. The same year, in Uganda, Trypanosomes are discovered in the cerebro-spinal fluid (CSF) of sleeping patients. For the researchers of the time, he is the person responsible for sleeping sickness. They conclude that there are in fact two distinct Trypanosomes: one in the blood, not very pathogenic, and another in the CSF and real sleeping sickness. The other researchers noted that blood Trypanosomes are present only in areas where sleeping sickness occurs as they are in all respects identical to those found in thenervous system. They conclude that the Trypanosome found in the blood is the first stage of sleeping sickness. Knowing that this disease evolves in two periods and that the Trypanosome is the pathogen, it remains how to discover its transmission. This is done by Bruce (1903), who suspects tsetse flies to be the vectors of the disease, provided experimental proof of this by transmitting Trypanosomes to animals through wild flies fed on sleepers.

2.2.2. Generality of African Human Trypanosomiasis

Vector

The tsetse fly or the tsetse fly has a biological and demographic group feature, it is important in medicine, when it comes to talking about HAT, it has biological and demographic characteristics that give it a unique place among the medically important vectors. She has a particular evolutionary cycle by anal way. It does not give eggs, but produces only one larva that grows in its uterus. This larva receives its food from the uterine glands of the mother ("adenotrophic viviparity") and when it has reached maturity (third instar larva), it settles in moist soil. Underground quickly it changes stage and becomes; the adult insect about 20 to 80 days later, their longevity depends on the environment they live in, the hottest time reduces the life span. (The development of the pupa is better with temperatures below $16 \degree C$ or above $36 \degree$)



Figure 2.1Glossina during a blood meal (Warren Photographic, 2014)

a) Risk Factors

The transmission it is depend of the location, population of tsé-tsé flies, occasion of contact human tsé-tsé, their longevity, frequency of blood meal and number of tsé-tsé being infected.

b) The transmission of THA

Transmission is done by tsetse flies (its vector) find suitable habitats. The tsetse flies havean ecological who allows interaction with humain. The DRC with immense forest and riparian resources offers a very favorable environment for the evolution of tsetse flies and promote Trypanosome transmission.

The life cycle is very important to know biology andepidemiology. T.b. Gambiense istransmitted to human subjects by the bite of infected tsetse flies. Transmission occurs during human-tsetse meeting the rural environment when they go to forest for, agriculture, hunting, fishing and breeding are practiced. The time do they get their maturation several factors and are particularly sensitive to temperature (Macleod et al.,

2007). It is in news born flies during their bites that the risk of being infected is maximal. Once infected, a fly stays for the rest of his life. We think that the young flies that are susceptible to infection and most ingested Trypanosomes are not able to develop, it is important to know also the maximum duration of life of an infected fly and what the daily frequency of meals.

c) Evolutionary cycle of Trypanosoma Brucei.

Trypanosomes of the T. brucei group are transmitted by the tsetse flies or tsetse flies that belong to the genus Glossina. Their life cycle is relatively complex, and this cycle occurs in the digestive tract of the vector with various stages that exhibit distinct biochemical morphology and physiology in mammalian hosts and vector insects.

Sexual reproduction is not necessary in Trypanosomes. However, it is produce in the body of the tsetse fly in his intestine immediately newborn go to stay in salivary glands and there is production of classical form called haploid gametes. In this stage, there is important transfert of genetic materialgenetic and allows rapid evolution and acquisition of important characteristicas drug resistance and human pathogenesis. The life cycle begins with the inoculation, during the bite of a tsetse fly, of meta-cyclic forms prefered to live in the bloodstream. These metacyclic forms are differentiated by givebirth to blood-forming forms proliferative long and slender, which multiply in the blood and other liquids of the body. They go up in the central nervous system, leading to the second stage; these forms give neuropsychiatric complication, and many other troubles of the disease. The procyclic form, which reproduces in the midgut of the insect, migrates to the salivary glands where it undergoes differentiation into infectious metacyclic form, characterized by the acquisition on its surface of a protective coating formed of

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glycoproteins that will allow it to survive once passed on to its human host. There are other forms of tsetse fly that are difficult to cultivate in the laboratory and remain poorly known. This unknown mechanism may pose a problem for researchers in case of examples of resistance to certain drugs by such strains (Peacock et al, 2011).

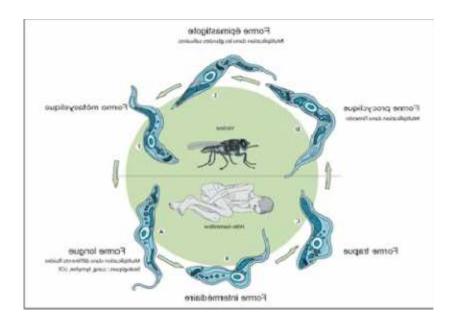


Figure 2.2 Evolutionary cycle of Trypanosoma Brucei

2.2.3.Clinical forms

Clinically, there are two phases of HAT, the first phase or lymphatico-blood and the second is the meningoencephaliticphase.

Exhaust Immune System

The pathogenic microbial agent develops certain mechanism to survive within host, during his evolution to kill germs. As noted above, infectious Trypanosomes for humans are able to escape the activity of non-immune trypanolytic factors present in the blood.These microorganisms are, however, highly immunogenic and elicit an immune response in the form of antibodies belonging in particular to the class of immunoglobulins IgM and IgG

2.2.3.1.Lymphaticoblood phase (first phase)

According to this phase the parasite is finding in lymphatic-blood system. The parasite can survive during six to three years. This leads to the chronicity of diseases. The duration of 3 years is an average for these phases. Exceptionally, there is a canker of inoculation on the site of the piquire. The main manifestations of this phase are: long-term and repeated fever, headache, pruritic itching, cervical adenitis, weakness, general asthenia and anemia and, rarely, hepatosplenomegaly. During this phase, can observe some minor symptoms and often this is not a reason for consultation of the doctor by patients. It is this clinic that is aspecific that makes the disease is tracked late and evolved chronicity. (Checchi et al., 2008)

2.2.3.2. Neuropsychiatric Phase (second phase).

HAT causes meningoencephalitis that affects different areas of the brain. No specific neurologic or psychiatric symptoms such as headaches or mood or behavioral disturbances are frequently observed during the first and second phases, but their intensity and persistence increase as the disease progresses (Blum et al. al., 2006). Once the parasites have crossed the blood-brain barrier and invaded the central nervous system, the clinical manifestations correspond in part to the location of the brain lesions. For example, sleep disorders can be explained by supraoptic nuclei, extrapyramidal hyperparous disturbances due to involvement of the thalamus and associated structures.

Deep sensory disturbances are one of the hallmarks of the disease. The pain is sharp at the slightest shock.

This event is known as the Kerandel Key. In terms of surface sensitivity, paresthesia, hyperesthesia, anesthesia and pruritus are often referred to (Kennedy PG, 2006). Abnormal movements and disturbances of tone and mobility are frequently observed in advanced cases; they are the manifestation of lesions in the diencephalon and the upper part of the middle brain. Motor weakness, tremors, bradykinesia and common symptoms. Signs of extrapyramidal disorders sometimes predominate with parkinsonian stiffness and paratonia.

Bad movements may be choreetetotic and mainly involve the distal extremities of the extremities of the upper limbs. Cerebellar involvement may be suspected in patients with ataxia and abnormal gait. Hemiplegia is rare and usually occurs at a very advanced stage. We can also observe the presence of archaic reflexes such as the reflex of the pout and palmo-chin reflex. Mental disorders can occur early in the first phase and lead to the diagnosis of primary psychiatric illness (Urech et al., 2011). Mood disorders such as irritability or indifference, aggressive or antisocial behavior, exuberance or apathy, depressive and delusional states with hallucinations are frequently observed. In the terminal stage, serious disorders of consciousness, with symptoms of dementia and epilepsy, manifest themselves by incontinence, coma, malnutrition, cachexia, ulcerative pressure, bacterial superinfections (aspiration pneumonia) and the death.



Figure 2.3. Patient at the terminal stage./ Figure 2.10: Coma.

) Endocrine disorders

They are not need a specific treatment. There is a decrease in pituitary gonadotropins (follicle-stimulating hormone or luteinizing hormone) in 50% of women and testosterone in 50% of men, leading to sterility in some couples. Amenorrhea, loss of libido, and sexual impotence were also observed. The circadian rhythm of the secretory hormone, including prolactin, renin, growth hormone and cortisol, disappears in severe cases. Hence the importance of a well-managed treatment to save the patients from these complications. Thyroid or adrenal disorders can cause goiter, overweight and diabetes.

2.2.4. DIAGNOSIS

Clinical signs and symptoms are not sufficient to decide on treatment in a HAT suspect. The traditional diagnosis of HAT is thus laboratory-based and involves several stages or a decision tree (Chappuis et al., 2005). With regard to T.b.gambiense, there is a series of tests to be performed. Any patient who has been diagnosed with the disease is called a HAT suspect and will be considered trypanosomatic only after the parasite is detected and the stage of the disease is determined. In these different tests, vector control activities should be intensified in risk areas ((Mitashi et al, 2012).

2.2.4.1. Antibody detection

Trypanosomes result in the production of antibodies with high concentrations of specific IgG and IgM that can be detected by the various serological tests.

The sensitivity and specificity of antibody screening depends on the type of antigens used. The large number of tests for the detection of antibodies against T.b.gambiense contains certain VSG glycoproteins corresponding to the variable LiTat antigens 1.3 and 1.5. The majority of patients infected with T.b. gambiense are carriers in their VSG bloodstream. Serologic testing does not have the ability to detect antibodies until 3-4 weeks after infection; this may be considered one of the reasons that there are sometimes false negatives. Regarding the diagnosis of T.b. Gambiense, there is a rapid agglutination test that is the most used among many others for mass screening. There are also rapid diagnostic tests that can be used for individual screening, which are still being tested in many endemic countries. Immunofluorescence or enzyme linked enzyme immunosorbent assays (ELISAs) require more laboratory infrastructure. In the DRC this test is used only at the reference laboratory level.

2.2.4.2. Card agglutination test for Trypanosomiasis

The card agglutination test for trypanosomiasis (CATT) is a simple and rapid test for the detection of specific antibodies to patients with T. b. Gambiense (Hasker et al., 2010). Because of its simple, reliability and low cost, it is used in all serological screening programs for populations at risk of transmission. The introduction of CATT in the mass screening of populations is a big step forward, which makes it possible to limit the long parasitological examinations to the cases of which the CATT gives a positive result. The CATT antigen consists of the variable LiTat-type 1.3 antigen of whole blood forms of T.b. Gambiense.

To prepare this antigen, the trypanosomes are extracted from the blood of infected rats and, after purification and fixation, stained with Coomassie blue and lyophilized.

The kits contain the reagent, the positive and negative control will be the material needed to perform the test on whole blood (capillary tubes, test cards, reagent mix sticks and samples, aspirating beads, syringe and dropper). For screening, the test is performed on undiluted whole blood (CATTsg). This test cannot be performed on the LCR. A heparinized capillary tube is filled with a drop of blood collected by fingertip puncture. For the agglutination test, a drop of CATT antigen is deposited during the examination of the plasticized card which is then placed on a rotary shaker at 60 rpm. The reading of the result is done after 5 minutes. In the presence of weak to very strong agglutination visible to the naked eye, the test is considered positive; if there is no visible agglutination, the test is negative. And one stops with the file of the patient, if positive one continues with the other investigations until the confirmation of the diagnosis.

2.2.4.3. Detection of the parasite

Detection of the presence of parasites is an important step in the confirmation of trypanosome infections and therefore constitutes the definitive diagnosis of HAT. Most techniques, except thick blood, rely on the visualization of trypanosomes because of their mobility. Parasitological diagnosis consists of a microscopic examination of the ganglionic fluid or blood and (CSF) examination is usually performed for the diagnostic phase, but this examination can also be used to diagnose HAT in highly suspect cases.

When other parasitological examinations are negative. The detection of the parasite may require a lot of work.

Some of these techniques have been published (Checchi 2011, Arbyn, 1993). For successful parasitological examination, the time elapsed between collection and examination should be as short as possible (<1h) to avoid the immobilization and lysis of trypanosomes. If, the examination can be done late, this must not exceed 48 hours since the taking.

Equipment maintenance, especially the microscope. For fresh preparations such as ganglionic fluid, and using techniques such as micro-micro-spin micro-column (mHCT), the microscope must be minimized by lowering the condenser and reducing the illumination.

The most sensitive techniques for detecting parasites should be used. Such mAECT on buffy coat), these techniques not only detect the parasite, but also determine the different stages of the disease and make a therapeutic decision.

) Ganglionic Juice

In the presence of engorged cervical ganglia, a puncture is performed to collect the liquid and deposited on a slide, then covered with a slide with which the sample is spread, the preparation then being examined under a microscope with a magnification of 40 x 10. Mobile trypanosomes. Because of its simplicity and low cost, this technique is widely used. Its sensitivity is about 59% (range: 43-77%) but depends on the proportion of HAT cases with enlarged lymph nodes, which can vary from one household to another (Ilboudo H et al, 2011) If the Catt is positive, the examination of the positive lymph node

fluid, the next examination will be to detect the parasite, then the stages of the disease and treat.

) Centrifugation in micro-hematocrit tubes

The capillary tube centrifugation or (Woo test). The capillary tubes containing an anticoagulant are filled to three quarters (about 50 μ l) with the blood collected by puncture at the end of the fingers. The dry end is sealed with modeling clay or a flame, being careful not to heat the blood to kill the trypanosomes. The trypanosomes are concentrated in the same layer as the leucocytes, between the plasma and the erythrocytes, by high speed centrifugation (12 000 g for 5 min) in a centrifugal hematocrit. This test is carried out in the DRC, when the Catt-test set positive and the ganglionic puncture is negative, then the recourse will be made to the Woo test.But it is not used at the health center.

) Buffy Coat Technique (QBC)

This technique, which was developed to diagnose blood parasites, including plasmodia and trypanosomes (Bailey JW, Smith DH, 1992), has been used successfully in the diagnosis of sleeping sickness. It combines the concentration of parasites by centrifugation and fluorescent staining of the DNA of the nucleus and the kinetoplast of living trypanosomes by the orange of acridine. It is a technique widely used in the DRC, it is one of the good methods, but its use is limited to the level of the general hospital.

) Technique of the mini-column anion exchange

Avec un pH de 8, les cellules sanguines sont à même de négativement que les trypanosomes restent neutres et peuvent être séparés par chromatographie d'échange d'anions. La technique consiste à faire passer 350 à 500 µl de sang sur une colonne de diethylaminoethylcellulose. Les cellules sanguines sont des voies sur legel et l'éluant contenant les trypanosomes qui sont collectés dans un tube. Les trypanosomes sont concentrés dans le tube par centrifugation à basse vitesse (1000 g pendant 15 min), après quoi le tube est examiné au microscope (grossissement 10 x 10 ou préférence 10 x 16) (Büscher et al. 2009). Cette technique est utilisée en dernier lieu, selon l'algorithme de diagnostic de la HAT en RDC.

) Polymerase Chain Reaction.

PCR produces billions of copies of short-term DNA sequences in 2 hours by a thermally cycling controlled enzymatic reaction. Several PCR-based assays have been developed for the detection of Trypanosozoon and there is a specific test of T.b. Gambiense that targets the TGSGP gene (In general, the amplified DNA is visualized by agarose gel electrophoresis followed by ethidium bromide staining.) Real-time PCR has been developed to allow high detection. Trypanosozoon DNA Stream (Becker et al., 2004) Tests were performed to simplify the detection of amplified DNA using a lateral flow test, the objective being the standardization of this test. This method also exists in the DRC, but only at the reference laboratory level for monitoring HAT.

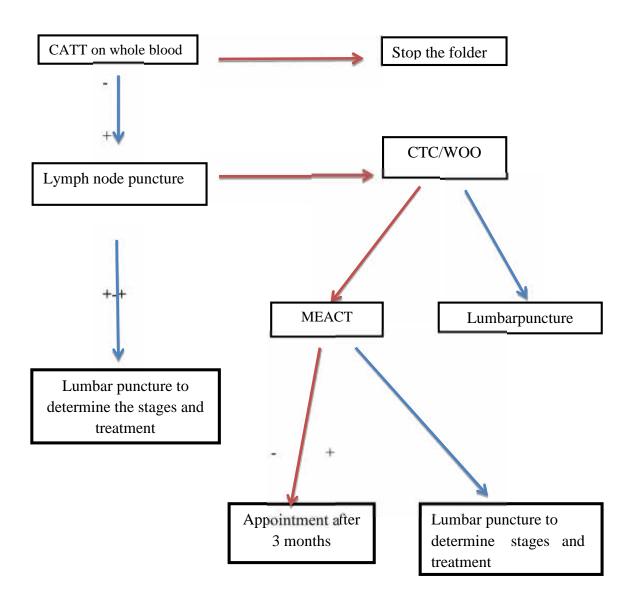


Figure 2.4. Thediagnosis algorithmof the HAT in DRC.

Comment:In the DRC, in order to carry out the fight against HAT successfully, passive screening is being integrated in some health facilities in endemic health zones of the THA, apart from active screening. A diagnostic algorithm has been adapted according to the epidemiological profile of the country.

The system works in this way, any patient who comes to consult should be sensitized to be tested for HAT.The first recommended examination is the Catt-test on whole blood, if the negative one, the file of the patient will be classified.

If positive, this one will pass to the ganglionary puncture, a positive, it will undergo a lumbar puncture to determine the stage of the disease, detection the trypanosome and finally to decide on the treatment. If the ganglionary puncture is negative, the recourse will be made to the CTC, in case of positivity of this examination the same schema above will be followed, if negative, the last recourse will be done this time to the MEACT, if positive the same logic will be followed, if negative, an appointment of three will be given.

2.2.5.Treatment

2.2.5.1. Treatment of the first phase

Currently, the treatment regimen used by most HAT control programs is to give injections for 7 days, with daily doses of 4 mg / kg of pentamidine isethionate. The drug is usually given as deep intramuscular injections, so intravenous injections frequently cause hypotension. If intravenous injection is used, avoid bolus injection and 60- to 120-minute infusions.

Pentamidine

Pentamidine, which appeared in 1940, is a synthetic aromatic diamine having a relative molecular weight of 340 g / mol for the base, 533 g / mol for methanesulphonate and 590 g / mol for isethionate. It is chemically related to the phenomenon, a diabetic.

The recommended dose has changed over time. There is a significant reduction in the amount of active molecule injected if isethionate (Pentacarinat®) is used rather than methanesulfonate (Lomidine®), whose production is dead (Dorlo TP & Kager PA, 2008). The pKa of 11.4 indicates that the vast majority of the drug is positively charged at physiological ph. This drug is used in the first phase of HAT disease, in the DRC, in case of failure of treatment we will resort to the schema NECT which is used in the second phase of the disease.

2.2.5.2.Treatmentof Second Phase of HAT

Nifurtimox-effornithine combination therapy (NECT) has been tested in a multicountry trial to compare the usual effornithine treatment with a combination nifurtimox and effornithine regimen to simplify treatment. Effornithine has a short half-life and its pharmacokinetics indicates that it requires four daily doses. It has been argued, however, that the short half-life of effornithine may be outweighed by its long acting pharmacodynamic effect on trypanosomes because T. b. Gambiense takes a long time (18 to 19 h) to reconstitute his ounce of ornithine carboxylase inhibited by effornithine; under these conditions, two daily doses may be sufficient (Priotto et al., 2007) .This therapeutic combination has come to bring a new breath in the treatment of HAT. Before its use it was mélarsoprol that caused many deaths by arsenic encephalopathy.

a) Treatment during pregnancy

There is less information about the treatment of HAT in pregnant women. No research conducted on anti-trypanosome treatment during pregnancy and lactation (Nadjm et al., 2009). The following recommendations are based on clinical practice

rather than solid evidence. For a T. b. Gambiense in pentamidine may be given in the first phase after the first trimester; if the patient has not completed the first trimester, this drug is contraindicated to be until the second trimester. For a T. b. Gambiense in second phase, melarsoprol, effornithine and nifurtimox are in principle all contraindicated and the timing of treatment depends on the general condition of the mother. Normally the treatment is contraindicated, but it depends on the General state of the gestante.In case of emergency, it is necessary to explain to the members to decide between losing their sister and taking risk of an abortion.

NECT will be after delivery. If the general condition of the mother is moderately or severely impaired, effornithine or NECT monotherapy should be given, the main objective being to have the mother this time. The patient and those close to them should be informed of the risks and benefits expected from the treatment.

Diseases and phase	Treatment of	Dosage	Other treatments
HAT à T.b.	first intention		
gambiense			
First phase	Iséthionate of	4 mg /by kg /per day	
Leucorachie :	pentamidine	over 7 days in	
0-5/µl		intramuscular or	
		intavenous. (diluted in	
		physiological solution	
		infusion of 2h)	
Second phase	Combined	Eflornithine: 400 mg / by	Eflornithine: 400
Leucorachie :	Treatment	kg / per day intravenous	mg / kg / day
6–20 /µl,	nifurtimox +	two infusions of 2h (each	intravenous in 4
>20 /µl,	eflornithine	dose diluted in 250 ml of	infusions of 2h
		water) over 7 days	(each dose diluted
			in 100 ml of water)
		Nifurtimox: 15 mg / kg	during 14 days.
		/per day oral voice in 3	second intention
		doses during 10 days.	(eg:melarsoprol: 2.2
			mg /by kg / per day
			intravenous during
			10 days

Table2.1. Anti-Trypanosome treatmentforthe first and second phase.

2.2.6. Evaluation of the results after treatment

After the treatment of HAT, 10 or 14 days, at the exit of the care unit, the patient receives a schedule for control, every six months and up to 24 months after treatment (Lejon and Büscher, 2005). That said, the rate of relapse after treatment of the first phase of T. b. Gambiense pentamidine is less than 5% (Eperon et al., 2007, Balasegaram et al., 2006). In addition, for the second phase, treatment with nifurtimox-eflornithine is used to treat 98% of patients; the relapse rate is less than 2% (Priotto et al., 2009, Franco et al., 2012).). In practice, follow-up recommendations are poorly observed by patients and they rarely return spontaneously for re-examination after their first follow-up visit, especially if they are asymptomatic (Hasker et al., 2012).It is depends to country. In the DRC, the patients scrupulously respect the appointment. After two controls, if there is presence of the parasite they will declare that there is relapse and the patient will be sensible to resume treatment according to its stage.

2.3. Preventive measures of hat

2.3.1.Trapping system

Traps are volumes within which the tsetse fly must enter. It is killed either by prolonged exposure to the sun or by contact with an insecticide deposited in the tissues that compose it. Many tsetse flies do not enter traps, but settle on outside tissues. This justifies that all traps are impregnated with an insecticide, at least once before laying. Contact with the insecticide will kill them, at least as long as the insecticide is still active.Several models of traps have been invented, but they will not mention the traps for tsetse flies of veterinary interest, nor traps too complex to build, nor those that have not

been tested on a large scale. This is the technique by excellence that is used in the DRC to lead the fight against vector.



Figure 2.5. Traps Pyramidal (Bouyer et al. 2005)

2.4.Review of previous studies

2.4.1.Study in Uganda

Studies in Uganda report a significant lack of correlation between CATT on blood and PCR (Kyambadde et al.,2000). In Côte d'Ivoire, however, problems of reproducibility of PCR from blood have been demonstrated (Garcia et al, 2003). In seropositive individuals with negative parasitological examination, two successive PCRs do not give same result. Longitudinal follow-up of these cases shows that positive PCR results occur less often in a seropositive population (defined as serologically positive at each of the six follow-up visit) than in a population of seronegatives (defined as serologically negative at least 1). One of six visits), (Magnus et al., 2000).

Finally, on blood samples of seropositive individuals not confirmed on parasitological examination, discrepancies are found according to DNA extraction methods.

2.4.2 Study In Cote D'Ivoire

Côte d'Ivoire, in the post-crisis context, passive surveillance is mainly based on the Daloa Clinical Trypanosomiosis Research Project (PRCT), which is currently the only operational center for passive screening and treatment of HAT. Two other "peripheral" centers also have the capacity to detect Trypanosomes: the Sanitary District of Sinfra and the Bonon Urban Health Center, areas that have suffered the two most recent outbreaks of HAT. It is also mainly in these homes that the medical surveys conducted by the PNETHA teams and its partners, the Pierre Richet Institute (IPR) and the PRCT are focused.

With regard to the phase diagnosis of the disease, the positivity of the CSF PCR signifies the presence of the parasite in the CSF and decides to treat all positive subjects with melarsoprol. However, in a recent study conducted in Côte d'Ivoire, several subjects whose CSF PCR was positive, but the negative DC and the number of cells between 0 and 5, were effectively treated with pentamidine (Garcia et al, 2003). In addition, subjects with 0 to 20 cells / μ l or positive DC could be treated effectively with pentamidine, suggesting that even the presence of trypanosomes in CSF does not seem to justify the use of melarsoprol (Doua et al., 1996). Although PCR / LCR can improve the phase diagnosis of the disease, its Interest does not always appear obvious in the therapeutic decision. For that, what is important is to have an idea about the evolution of the patients during the follow-up phase, their serology.

2.4.3.Burkina Faso

In Burkina Faso, imported cases from Côte d'Ivoire can potentially spread throughout the country. One of the passive strategies gradually put in place in recent years by the PNLTHA is to regularly sensitize and train, at the national level, the medical personnel best able to diagnose and treat these cases. Once a case is identified, it is necessary to check whether its environment is suitable or not (presence of tsetse in the area) to a possible transmission of the parasite.

If this is the case, a proximity survey is conducted to verify that population sharing the same spaces as the trypanosome has not been infected. The other strategy is to carry out medical surveys in areas of re-emergence risk identified from several criteria: history of the disease, agricultural zone of the zone, hydrographic network, presence of tsetse flies, presence of returnees (Courtin et al., 2010).

CHAPTER THREE

METHODS AND MATERIALS

3.1. Study Area

In this study, investigations are conducted in the Democratic Republic of Congo. Precisely in the city of Bandundu, chief-town of Kwilu province. This city formerly called Banning-city has a population of 950,683 inhabitants, with an area of 222 km². It was created by the ordinance number 69-275 of November 21, 1969. This study is geographically restricted in the Bandundu health zone, where the PNLTHA provincial coordination is located, and the surveys focused on Bandundu mobile team data for three years (from 2015 to 2017).

3.2. Geographic Location

The city of Bandundu is bounded: To the east and south of the territory of Bagata with as limits, the village Bonkulu, the river Kolumulua and the river Kwilu.To the north by the territory of Kutu which is in the province of Mai-ndombe, with the river Kasai as common border.To the South by the territory of Kwamouth with as a natural boundary the river Kwilu.To the west and south the territory of Mushie.The city of Bandundu has a type of tropical climate, rains are common. It has two seasonal variations: dry and rainy. The dry season starts on May 15 and ends on September 15 and the rainy season starts on September 15 and ends on May 15 after being cut by a small dry period of about 1 month between January and February.

3.3. Work Methodology

This cross-sectional descriptive survey of the situation of Trypanosomiasis diagnosed at the first stage of HAT during the period from 2015 to 2017. This survey took place in the city of Bandundu, capital of the province of Kwilu which is one of the twenty-six new provinces in the DRC. The said province has two coordination of the national program for the control of HAT, the Bandundu / North coordination which has 7 mobile teams and 6 CDTC in the city was targeted to collect the data.

The population of the study consists of trypanosomatic patients of Congolese nationality, consulted and diagnosed by the mobile team in Bandundu town and the health facilities that integrated the serode de-screening (general hospital and health centers) during this period. The variables of the study are: sex, age of patients of 0-4 years, of 5- 14 years and 15 years and more per year. It will have to present the number of villages and health areas endemic, by zone of health endemic, compare the number of cases diagnosed according to the two strategic approaches (passive and active) at the first stage of HAT. Annual prevalences of the disease are also calculated.

3.4 Ethical considerations

The data presented in this study do not suffer from an ethical problem, since they do not directly or indirectly implicate the privacy of the patients, nor the professional secrecy of the health institutions of the community.

Although the authorization of the ethics committee of the place was solicited and acquired to allow the researcher wanting to contribute to the improvement of the health situation related to the HAT.

3.5.Data collection and analysis

To successfully carry out this study, the raw data were entered and the prevalence calculation was done in Excel 2010 and analyzedby (SPSS, version 20). Statistical analysis such as, the test of chi-square was done to establish the relationship between the number of patients diagnosed at the first stage, according to the two strategic approaches (passive and active). The level of significance used in the study was 0.05.

3.6.Research Method

The test for a statistical significance in order to determine if the outcome of an event is attributable to some factors or an intrinsically attributed to some chance is a vital tool in various fields of studies especially in the health sciences. There are many analytical methods to establish this diagnostic relationship of cause and effects dependency and of such is the Chi-square statistical test.

3.7.Chi-Square TestMethod

The Chi- Square is a statistical test of significance developed by Karl Pearson to compute the total differences between the expected and observed count/frequency of observations in a table with cell units.In a most comer use, it is used to examine if variables with a categorical outcome have sort of association/dependence on one another or they are statistically independent (Robert, n.d). The Chi Square test is based on the concept of a cross tabulation or contingency table. The contingency table involves a combined frequency distribution of categorical variables into unique cases. In order to determine if the joint frequency distribution of the cases is statistically associated or independent, the Chi–square Statistic(2) is used to examine this relationship. Furthermore, in the case of established dependency, a further test statistic such as Phi correlation and Crammers' V measures and so on can help examine the extent of the relationship magnitude (Robert, n.d).

Some of the basic assumptions underlying the use of Chi- Square statistical tests are: The variables must be categorical in nature(usually in a nominal scale); the observations should be randomly independent; Random sampling of observations are not strict to be considered; all categories of units are expected to include their respective observations. Empty cells in the contingency table will hinder a Chi-Square test; the expected frequencies of each cell need to be moderately large. The expected frequencies of each cell should be range from 1 and above and also, 20 % of the expected frequencies should not be lower than 5.

The Chi-Square Statistics can be stated as follows:

 $2 = \sum ((O-E)^2)/E$

O= the Observed Frequency

E = the Expected Frequency

The Expected Frequency computation formula is given as:

$$\operatorname{Eij} = \frac{T XT}{N}$$

Eij = the expected frequency in the ith row and jth column

Ti = Total number of sum in the ith row

Tj= Total number of sum of the jth column

Ni= Total number of sum in the table

The degrees of freedom are equal to (r-1) (c-1), where r is the number of rows and c is the number of columns.

The decision rule for the rejection of the null hypothesis (There is no dependent association between the variables of interest) is that the p-value computed must be greater than the level of significance(). Due to the advancement in statistical computing, there are several statistical packages that can compute the Chi-Square Test Statistic rather than have it done with manual computations.

CHAPTER FOUR

RESULTS

4.1. Statistical presentation of participants' results

Variable		n	%
Gender	Female	169	63.30%
	Male	98	36.70%
Village	Bandundu	107	40.10%
	Kilongo	117	43.60%
	Kagata	21	7.90%
	Kwamouth	22	8.20%
Screening	Passive	117	43.80%
	Active	150	56.20%
Stage	First	178	66.70%
	Second	89	33.30%

 Table 4.1. Descriptive Statistics of the Participants (N=267)

In order to examine the hypotheses of no significance difference and independence between selected variables, the Chi – Square Test was used and the coefficient of relational strength between the variables was computed to measure the strength of the relationships.

4.1. Chi -square test on gender and screening type

Hypothesis Statement

- H_o: Gender and Screening Methods are independent
- H₁: Gender and Screening Methods are not independent

Decision Rule: H_0 is not assumption if p-value < 0.05

Variable		SCREENING					
	_	Passive screening		Active screening			р
Gender		n	%	n	%		
	Female	78	46.2%	91	53.8%	1.019	0.313
	Male	39	59.8%	59	60.2%		

Table 4.2: Chi-Square Test of Gender versus Screening

The Table 4.2 above shows that female participants (53.8%) undergo more of active screening while 46.2% of the female participants partook in a passive screening method. In the male category, male participants (60.2%) partook also more on the Active screening while less of them (39.8%) undergo passive screening. In contrast, it appears that more of male participants took part in Active screening than their female counterparts. However, these differences are not statistically significant as shown by the Chi-Square Test value. Since the Chi Test revealed that the p-value > 0.05, the H_o is accepted. Therefore, it can be concluded that the Gender and Screening Methods are independent. That is, being a male or a female does not have any statistically significant effect on what screening method is being undertaken.

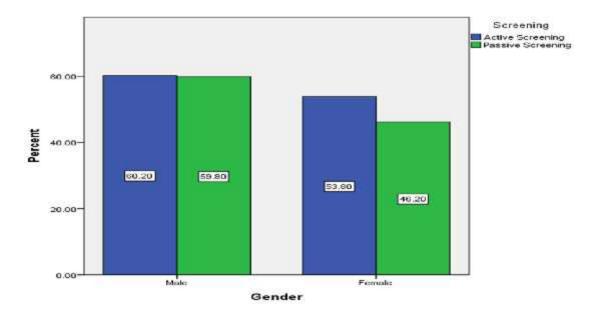


Figure 4.1: Barchart of Gender with Screening Type

4.2. Chi square test on gender and screening type

Hypothesis Statement

- H₀: Gender and Stage are independent
- H₁: Gender and Stage are not independent
- Decision Rule: H_o is not assumption if p-value < 0.05

Variable		Stage					
-		Stage 1		Stage 2		2	n
Gender		n	%	n	%	2	р
F	emale	120	71.%	49	29.%	3.901	0.048
Ī	Male	58	59.2%	40	40.8%		

Table 4.3. Chi-Square Test of Gender versus Stage

The table 4.3 above shows that 71% of the female were considered to be in the stage one when screened while 29% of the remaining were in the stage two when screened. 59.2% of the male participants were screened as stage one while 40.8% of the remaining were found to be the stage two when screened.

Since the p-value < 0.05, the null hypothesis (H_o) is not assumption. Therefore, it can be concluded that Gender and Stage are not independent (2 (1) = 3.901, p < 0.05). That is, being a male or a female does have a statistically significant effect on what stage they could be when screened.

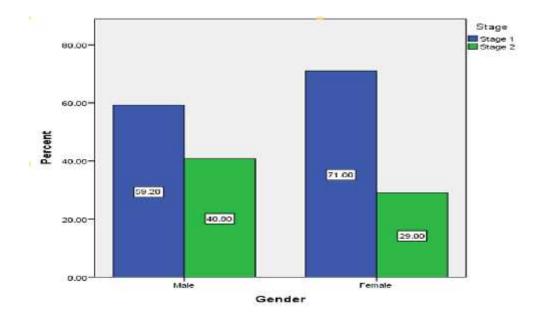


Figure 4.2: Barchart of Gender with Stage Type

4.3. Chi square test on village and screening type

Hypothesis Statement

- H_o: The Participant Villages and the Screening types are independent
- H₁: The Participant Villages and the Screening types arenot independent

Decision Rule: H_o is not assumption if p-value < 0.05

Variable			Screening				
		Passi	ve	Active		2	р
Village		n	%	n	%		
	Bandundu	59	55.1%	48	44.9%	27.480	<0.001
	Kikongo	40	34.2%	77	65.8%		
	Bagata	20	9.5%	19	90.5%		
	Kwamouth	16	72.7%	6	27.3%		

Table 4.4: Chi-Square Test for Village versus Screening

From the table 4.4 above, it can be observed that 55.1% of the people from Bandundu took part in the Passive screening while 44.9% of them took part in the active screening. About 65.8% of people from Kikongo took part more in the Active Screening while 34.2% of them took part in Passive Screening. About 95.5% of people from Bagata took part in the Active Screening while 9.5% of them took part in Passive Screening. About 72.7% of the people from Kwamouth took part in the Passive Screening while 27.3% of them took part in the Active Screening Exercise.

Since the p-value < 0.05, the null hypothesis (H_o) is not assumption. Therefore, it can be concluded that the Village and Screening Types are not independent (2 (3) = 27.460, p

<0.001). That is, the type of village of the participants tends to influence the types of the Screening method they went for.

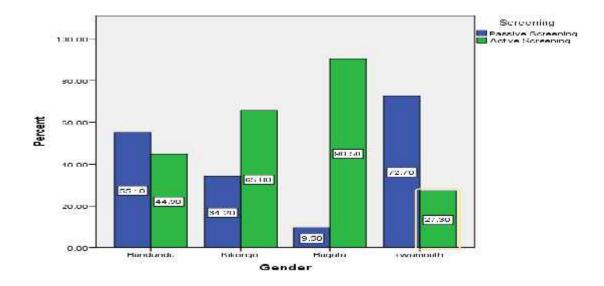


Figure 4.3: Barchart of Village with Screening Type

4.4.Chi square test on village and stage type

Hypothesis Statement

- Ho: The Participants' Village and the Stage type are independent
- H₁: The Participants' Village and the Stage type are not independent.

Decision Rule: H_o is not assumption if p-value < 0.05

Variable	e		Stage				
		Stage	1	Stage	2	2	р
Village		n	%	n	%		-
	Bandundu	57	53.3%	50	46.7%	17.135	0.001
	Kikongo	87	74.4%	30	25.6%		
	Bagata	19	95.5%	2	9.5%		
	Kwamouth	15	68.2%	7	31.8%		

Table 4.5. Chi-Square Test for Village versus Stage

From the table 4.5 above, it can be observed that 53.3% of the people from Bandundu were found to be screened as Stage 1 while 46.7% of them were found to be screened to be in Stage 2. About 74.4% of people from Kikongo were found to have a Stage 1 outcome while 25.6% of them were found to have a Stage 2 outcome. About 95.5% of people from Bagata have a Stage 1 screening outcome while 9.5% of them have a Stage 2 outcome. About 68.2% of the people from Kwamouth were found to have a Stage 1 screening outcome while 31.8% of them have a Stage 2 outcome screening process.

Since the p-value < 0.05, the null hypothesis (H_o) is not assumption. Therefore, it can be concluded that the Village and Stage Type are not independent (2(3) = 17.135, p < 0.001). That is, the type of village of the participants tends to have a statistically association effect on the type of Screening Stage outcome.

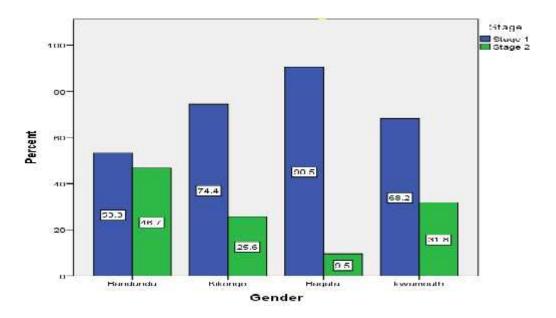


Figure 4.4: Barchart of Village with Stage Outcome

4.5. Chi square test on screening and stage type

Hypothesis Statement

- H_o: The Screening Type and the Stages 'outcome is independent
- H1: The Screening Type and the Stages' outcome arenot independent

Decision Rule: H_o is not assumption if p-value < 0.05

Variable		Stage					
		Stage 1		Stage 2		2	D
Screening	5		%	n	%		r
	Passive	61	52.1%	56	47.9%	17.135	<0.001
	Active	117	78%	33	22%		

From the table 4.6 above, it can be observed that 52.1% of Passive Screening participants have a Stage 1 outcome while 47.9% of them were found to be screened to

have a Stage 2 outcome. About 78% of people that undergo active screening werefound to have a Stage 1 outcome while 22% of them were found to have a Stage 2 outcome. It can be observed that Active Screening participants tend to have a Stage 1 outcome while passive screening participants tend to have more of Stage 2 Outcome.

Since the p-value < 0.05, the null hypothesis (H_o) is assumption. Therefore, it can be concluded that the Screening method and Stage Type are not independent (2 (1) = 19.785, p < 0.001). That is, the type of screening method used by the participants tends to have a statistically significant association with the Stages' outcome.

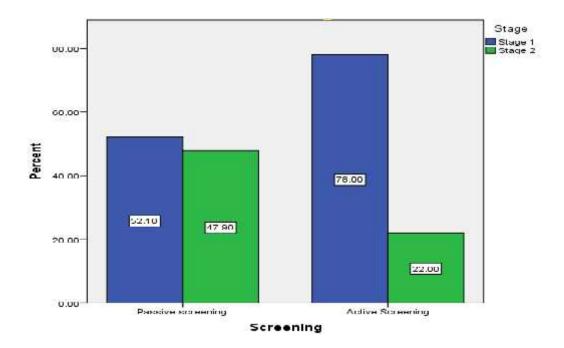


Figure 4.5: Barchart of Screening Method with Stage Outcome

CHAPTERFIVE

5.1. CONCLUSION AND RECOMMENDATIONS

HAT is a major public health problem in the DRC, given the number of cases reported per year, with insufficient integration of diagnostic structures. Between 1885 and 1920, this parasite ravaged the Congolese population, causing the desolation, sadness of many families; this situation had led to depopulation of some parts of the country, especially villages along the Congo River.

From the year 2015 to 2017, 267 new cases were detected with an incidence of 0.06%, by the Bandundu mobile team, in the Bandundu / Nord coordination.From the total 267 cases, 169(63, 3%) people were female while 98(36.7%) were male. The Kikongo village has the highest cases reported of about 117 (43.6%) cases closely followed by the Bandundu village with 107(40.1%) cases. The lowest reported cases are from Bagata Village and Kwamouth Village with 21(7.9%) and 22(8.2%) cases respectively. Passive screening cases were 117(43.8%) while the Active screening was 150 (56.2%) cases. Of all the screened cases, 178 (66.7%) were reported to be first stage while 89 (33.3%) cases were screened as second stage.

The analysis shows that female participants (53.8%) undergo more of active screening while 46.2% of the female participantstook partin a passive screening method. In the male category, male participants (60.2%) took part also more on the Active screening while less of them (39.8%) undergo passive screening. It was however found that Gender does not have a statistically significant effect on the screening method utilized. The study found that 71% of the female were considered to be in the stage one

when screened while 29% of the remaining were in the stage two when screened. 59.2% of the male participants were screened as stage one while 40.8% of the remaining were found to be the stage two when screened. The study found that being a male or a female does have a statistically significant effect on what stage they could be when screened.

The study shows that 55.1% of the people from Bandundu took part in the Passive screening while 44.9% of them took part in the active screening. About 65.8% of people from Kikongo took part more in the active screening while 34.2% of them took part in passive screening. About 95.5% of people from Bagata took part in the active screening while 9.5% of them took part in passive screening. About 72.7% of the people from Kwamouth took part in the Passive Screening while 27.3% of them took part in the Active Screening Exercise. Conclusively, the study show that the type of village of the participants tends to influence the types of the Screening method they went for. So it can be concluded that screening approaches (active and passive approaches) are different from one health zone to another.

The research findings deduced that 53.3% of the people from Bandundu were found to be screened as Stage 1 while 46.7% of them were found to be screened to be in Stage 2. About 74.4% of people from Kikongo werefound to have a Stage 1 outcome while 25.6% of them were found to have a Stage 2 outcome. About 95.5% of people from Bagata have a Stage 1 screening outcome while 9.5% of them have a Stage 2 outcome.About 68.2% of the people from Kwamouth were found to have a Stage 1 screening outcome while 31.8% of them have a Stage 2 outcome screening process. Conclusively, it found that the type of village of the participants tends to have a statistically association effect on the type of Screening Stage outcome. Bagata screened patients are found to have more stage 1 screening outcome.

The study also found that the type of screening method used by the participants tends to have a statistically significant association with the stages' outcome. It can be observed that Active Screening participants tend to have a Stage 1 outcome while Passive Screening participants tend to have more of Stage 2 Outcome.

According to this study, screening and diagnosis of HAT is a major element in any fight against HAT. The demonstration of trypanosomes in different biological fluids allowsconfirmation diagnosis of HAT. At the absence of identification of the parasite, the therapeutic decision will not be made.

Therefore, to successfully fight against HAT, we must use both strategic approaches (active and passive), combined with intense vector control, to reduce morbidity andmortality from HAT and hope eliminate this parasitosis by 2020 in the Democratic Republic of Congo.

Recommendations

To the National program of the Controlof HAT

To seek to extend the sero- screening to 50% in areasof endemic of HAT.

To reinvigorate the fight against vector by working in collaboration with the community.

REFERENCES

Abel PM et al (2004), Retaking sleeping sickness control in Angola. Tropical and International Health, 9:141–148.

A.BUGUET, R.CESPUGRIO, B.BOUTEILLE (2015), Trypanosome Humaine Africaine.

Ancelle T et al. (1997) Détection des trypanosomes dans le sang par la technique du quantitative Buffy coat; Médecine Tropicale, 57:245–248.

Apted FIC. George Allen and Unwin (1970), Clinical manifestations and diagnosis of sleeping sickness. In: Mulligan HW, Ed. The African trypanosomiases. London: 661–683. Asonganyi T et al (1991), Reactivation of an old sleeping sickness focus in Mamfe (Cameroon): epidemiological, immunological, and parasitic findings. Revue d'Epidémiologie et de Santé Publique, 39:55–62

Arbyn M. (1993), Etat actuel de la connaissance sur les méthodes de dépistage et de diagnostic de la maladie du sommeil [Current knowledge of methods for detecting and diagnosing sleeping sickness]. Antwerpen, Instituut voor Tropische Geneeskunde.

Balasegaram M et al. (2006), Treatment outcomes and risk factors for relapse in Patients with early-stage human African trypanosomiasis (HAT) in the Republic of the Congo. Bulletin of the World Health Organization, 84:777–782.

Baker N et al. (2012), Aquaglycéroporine 2 controls susceptibility to melarsoprol and pentamidine in African trypanosomes. Proceedings of the National Academy of Sciences of the United States of America, 109(27):10996–11001.

Bailey JW, Smith DH. (1992), The use of the acridine orange QBC technique in the diagnosis of African trypanosomiasis. Transactions of the Royal Society of Tropical

Medicine and Hygiene, 86:630.

Balyeidhusa ASP, Kironde FAS, Enyaru JCK (2012), apparent lack of a domestic animal reservoir in gambiense sleeping sickness in northwest Uganda. Veterinary Parasitology, 187:157–167

Becker S et al. (2004), Real-time PCR for detection of Trypanosoma brucei in Human blood samples. Diagnostic Microbiology and Infectious Disease, 50:193–199.

Bendiner E, Pearce E. (1992), A 'magic bullet' for African sleeping sickness. Hospital Practice (Office edition), 27(1):207,215,218,221.

Berrang Ford L. (2007), Civil conflict and sleeping sickness in Africa in general and Uganda in particular. Conflict and Health, 1:6.

Berberof M, Pérez-Morga D, Pays E. (2001), A receptor-like flagellar pocket glycoprotein specific to Trypanosoma brucei gambiense. Molecular and Biochemical Parasitology, 113(1):127–138.

Black N, Donald A. (2001), Evidence based policy: proceed with care. British Medical Journal, 323:275–279.

Bouteille B et al (2010), cerebrospinal fluid B lymphocyte identification for diagnosis and follow-up in human African trypanosomiasis in the field.ATropical Medicine and International Health, 15:454–461.

Bukachi SA, Wandibba S, Nyamongo IK. (2009), The treatment pathways followed by cases of human African trypanosomiasis in western Kenya and eastern Uganda. Annals of Tropical Medicine and Parasitology, 103:211–220.

Blum J, Schmid C, Burri C. (2006), Clinical aspects of 2541 patients with second stage human african trypanosomiasis. Acta Tropica, 97:55–64.

Blum JA et al. (2008), Cardiac involvement in African and American trypanosomiasis . Lancet Infections Diseases, 8:631–641.

Blum JA et al. (2009), Cardiac alterations in humanAfrican trypanosomiasis (respect to the disease stage and antiparasitic treatment). PLoS Neglected Tropical Diseases, 3:e383.

Büscher P et al. (2009), improved models of mini anionexchange centrifugation technique diagnosis and staging. PLoS Neglected Tropical Diseases, 3:e471.

Büscher P, Gilleman Q, Lejon V. (2013), Novel rapid diagnostic tests for sleeping sickness.New England Journal of Medicine, 368:1069–1070.

Buguet A et al. (2005), Sleep structure: a new diagnostic tool for stage determination in sleeping sickness. Acta Tropica, 93:107–117.

Buguet A et al. (2001) La maladie du sommeil: trouble majeur des rythmes Circadien Medicine Tropicale, 61:328–339.

Brun R, Blum J, Chappuis F, Burri C. (2010), Human African trypanosomiasis. Lancet 375: 148–59.

Bucheton B, MacLeod A, Jamonneau V. (2011), Human host determinants influencing the outcome of Trypanosoma brucei gambiense infections. Parasite Immunology, 33:438–447.

Camara M et al. (2010) Sleeping sickness diagnosis: use of buffy coats improves the sensitivity of the mini anion exchange centrifugation test. Tropical Medicine and International Health, 15:796–799.

Chappuis F et al. (2005), Options for the field diagnosis of HAT. Clinical Microbiology Reviews, 18:133–146 Chappuis F et al. (2004) Card agglutination test for trypanosomiasis (CATT) end-dilution titer and cerebrospinal fluid cell count as predictors of HAT among serological suspected individuals in southern Sudan. American Journal of Tropical Medicine and Hygiene, 71:313–317.

Checchi F et al. (2011), Accuracy offive algorithms to diagnose gambiense HAT. PLoS Neglected Tropical Diseases, 5:e1233.

Checchi F et al. (2012), Prevalence and under-detection of gambiense HAT during mass Screening sessions in Uganda and Sudan. Parasites and Vectors, 5:157.

Cecchi G et al. (2009), Towards the Atlas of human African trypanosomiasis. International Journal of Health Geographics, 8:155

Claude Laveissiere etClaude Penchenier (2005), Manual of fight against the disease of the sleep.

Cordon-Obras C et al. (2009), Trypanosomabrucei gambiensein domestic Livestock of Kogo and Mbini foci (Equatorial Guinea). Tropical Medicine and International Health, 14:535–541.

Courtin F et al. (2009), Impacts observés des évolutions démo-climatiques sur la répartition spatiale des hommes, des tsé-tsé et des trypanosomoses en Afrique de l'Ouest. Courtin F et al. (2005), Towards understanding the presence/absence of HAT in a focus of Côte d'Ivoire: a spatial analysis of the pathogenic system. International Journal of Health Geographics, 4:27 (doi: 10.1186/1476-072X-4-27).

Courtin F et al. (2010), Updating the northern tsetse limit distribution in Burkina Faso impact of global change. International Journal of Environmental Research and Public Health, 7:1708–1719.

52

De Almeida PP, Ndao M, Van Meirvenne N, Geerts S. (1998) Diagnostic evaluation of PCR on dried blood samples from goats experimentally infected with Trypanosoma brucei brucei. Acta Trop; 70, 269–76.

Deborggraeve S et al. (2008), Molecular analysis of archived blood slides reveals an atypical Human Trypanosoma infection. Diagnostic Microbiology and Infectious Diseases, 61:428–433.

Deborggraeve S et al. (2012), Diagnosis of sleeping sickness: update and perspectives. XVIII International Congress for Tropical Medicine and Malaria, Rio de Janeiro, 23-27

Deborggraeve S, Büscher P.(2012), Recent progress in molecular diagnosis of Sleeping Sickness. Expert Review of Molecular Diagnostics, 12:719–730.

Deborggraeve S, Büscher P. (2010), Molecular diagnostics for sleeping sickness: where's the benefit for the patient? Lancet Infectious Diseases, 10:433–439.

De Koning HP.(2008), Ever-increasing complexities of diamidine and arsenical crossresistance in African trypanosomes. Trends in Parasitology, 24(8):345–349.

Dje NN et al (2002),), Geographic distribution of trypanosomes supported in Côte d'Ivoire from 1993 to 2000 (Bulletin of the Society of Exotic Pathology.

Doua F, Miézan TW, Sano JR, et al. (1996), The efficacy of pentamidine in the treatment of early-late stage Trypanosoma brucei gambiense trypanosomiasis. Am J Trop Med Hyg 55: 586-8.

Dorlo TP, Kager PA. (2008), Pentamidine dosage: à base/salt confusion. PLoS Neglected Tropical Diseases, 2(5):e225.

Ducloux, M, M. Eugene Jamot (1988): a son of Limousin [Eugene Jamot (1879-1937): at

his of the Limousin region]. Bulletin of the Society of Exotic Pathology and its Subsidiaries, 81:419–426.

Dukes P et al. (1984), A field comparison of seven diagnostic techniques for HAT in the Luangwa Valley, Zambia. Tropenmedizin und Parasitology (Stuttgart), 35:141–147.

Fèvre EM et al. (2005), A burgeoning epidemic of sleeping sickness in Uganda. Lancet, 366:745–747.

Gillet P et al. (2013), false positivity in non-targeted infections in malaria rapid diagnostic tests: the case of human African trypanosomiasis. PLoS Neglected Tropical Diseases, 7(4):e2180.

Garcia A, Jamonneau V, Magnus E, et al. (2000), Longitudinal survey of positive card agglutination trypanosomiasis test (CATT) but apparently aparasitemic individuals in Côte d'Ivoire: evidence for complex and heterogeneous population. Trop Med Int Health; 5: 786-93.

Ginoux PY, Frezil JL, Alary JC. (1982), La trypanosomiase humaine au moment du dépistage en République Populaire du Congo. Distribution des signes cliniques. Médecine Tropicale, 42:281–

Gómez-Rodríguez J et al. (2009), Identification of a parasitic immunomodulatory Protein triggering the development of suppressive M1 macrophages during African Trypanosomiasis. Journal of Infectious Disease 200(12):1849–1860.

Hana Talabani, Thierry Ancelle (2011), Le diagnostic de la trypanosomiase humaine Africaine (THA).

Hasker E et al. (2010), Diagnostic accuracy and feasibility of serological tests on filter paper samples for outbreak detection of T. b. gambiense Humain Trypanosomiasis.

54

American Journal of Tropical Medicine and Hygiène, 83(2):374–379.

Hasker E et al. (2011), Health care-seeking behavior and diagnostic delays for HAT in the Democratic Republic of the Congo. Tropical Medicine and International Health, 16:869–874

Ismael Zoungrana Eric (2009,2011), HAT. Research Institute for development (IRD). Symptoms (Lymphatic-blood phase), on the cerebrospinal fluid of sleeping sickness patients in Côte d'Ivoire. Trop Med Int Health 2003; 8: 1–6.

Jamonneau V, Solano P, Garcia A, et al. (2003), Stage determination and therapeutic decision in Human African Trypanosomoses: value of PCR and IgM quantification on the cerebrospinal fluid of sleeping sickness patients in Côte d'Ivoire. Trop Med Int Health; 8: 1-6.

Jamonneau V et al. (2011). Evaluation of the immune trypanolysis test performed on blood collected on filter paper. In: 31st Meeting of the International Scientific Council for Trypanosomiasis Research and Control in Bamako.

Jamonneau V et al. (2012),Untreated human infections byTrypanosoma brucei gambiense are not 100 % fatal. PLoS Neglected Tropical Diseases, 6(6):e1691.

Jamonneau B et al. (2004,), Mixed infections of trypanosomes in tsetse and pigs and their epidemiological significance in a sleeping sickness focus of Côte d'Ivoire. Parasitology. 129:693–702.

Kennedy PG. (2006), Human African trypanosomiasis—neurological aspects. Journal of Neurology, 253:411–416.

Kennedy P.G (2013), Clinical features, diagnosis, andtreatment of HumanAfrican Trypanosomiasis Lancet Neurol., 12, 186-194.

55

K. Tshimungu1 et al (2009), Epidemiological, Clinical and Socio-demographic Characteristics of Human African Trypanosomiasis (HAT) in the Kinshasa Region, Democratic Republic of the Congo.

Khonde N et al. (1995), Epidemiological evidence for immunity following Trypanosoma brucei gambiense sleeping sickness. Transactions of the Royal Society of Tropical Medicine and Hygiene, 89:607–611.

KyambaddeJW,Enyaru JCK, Matovu E,et al. (2000), Detection of trypanosomes in suspected sleeping sickness patients in Uganda using the polymerase chain reaction. B World Health Org, 78: 119–24.

Laveissiere (c), PENCHENIER (L). (2005). Manual of fight against the disease of the sleep. Paris: IRD Publishing; p. 48.

Leak S. (1998). Tsetse biology and ecology: their role in the epidemiology and control of trypanosomosis. Wallingford, Oxford shire, CABI Publishing.

Lejon V et al. (2002), IgM quantificationin the cerebrospinal fluidof sleeping sickness patients by a latex card agglutination test. Tropical Medicine and International Health, 7:685–692.

Lejon Vet al (2003), The challenge of trypanosoma brucei gambiense sleeping sickness diagnosis outside Africa.

Lejon V et al. (2006), Detection of trypanosome-specific antibodies in saliva, towards non-invasive non-invasive serological diagnosis of sleeping sickness. Tropical Medicine and International Health, 11:620–627.

Lejon V, Büscher P. (2005), Cerebrospinal fluid in human African trypanosomiasis:a key to diagnosis, therapeutic decision and post-treatment follow-up.Tropical Medicine and

International Health, 10:395–403.

Louis FJ, Simarro PP. (2005), Les difficiles débuts de la lutte contre la maladie du sommeil en Afrique équatorielle française, 65:251–257.

Lutumba P et al. (2006), Validity, cost and feasibility of mAECT and CTC as Confirmatory tests in the detection of HAT].Tropical Medicine and International Health, 2:470–478.

Mäser P et al. (1999), A nucleoside transporter from Trypanosoma brucei involved in drug resistance. Science, 285(5425):242–244.

Mitashi P et al. (2012), Human African trypanosomiasis diagnosis in first-line Health services of endemic countries, a systematic review. PLoS NeglectedTropical Diseases, 6(11):e1919.

Moore A et al (1999), Resurgence of sleeping sickness in Tambura County, Sudan. American, Journal of Tropical Medicine and Hygiene, 61:315–318.

Moser DR, Cook GA, Ochs DE, et al. (1989), Detection of Trypanosoma congolenseand Trypanosoma brucei sub-species by DNA amplification using the polymerase chain reaction. Parasitology; 99: 57-66.

Mpanya A et al. (2012), Should I get screened for sleeping sickness? A qualitative study in Kasai Province Democratic Republic of Congo. PLoS Neglected Tropical Diseases, 6:e1467.

Mugasa CM et al (2012), Diagnostic accuracy of molecular amplification tests for human African trypanosomiasis—systematic review. PLoS Neglected Tropical Diseases, 6(1):e1438

Mumba Ngoyi D et al. (2011), Prevalence of HAT in theDemocratic Republic of the

Congo. PLoS Neglected Tropical Diseases, 5:e1246.

Miézan TW et al, (1994). Evaluation des techniques parasitologiques utilisées dans le diagnostic de la trypanosomose humaine à Trypanosoma gambiense en Côte d'Ivoire [. Bulletin de la Société de Pathologie Exotique, 87:101–104.

Miézan TW et al. (2002), Trypanosomose humaine africaine en Côte d'Ivoire: caractéristiques après traitement. A propos de 812 cas traités dans le foyer de Daloa (Côte d'Ivoire) Bulletin de la Société de Pathologie Exotique, 95:362–365

Noni MacDonald, MD(2014), La maladie de Chagas /trypanosomiase humaine Americaine.

Noireau F, Lemesre JL, and Nzoukoudi MY, et al. (1988), Serodiagnosisof sleeping sickness in the Republic of the Congo: comparison of indirect immunofluorescent antibody test and card agglutination test. Trans R Soc Trop Med Hyg; 82:237-40.

Paquet C et al. 1995), (La Trypanosomiase à Trypanosoma brucei gambiense dans le foyer du Nord-Ouest de l'Ouganda. Bilan de 5 années de lutte (1987–1991), 88:38–41.

Pépin J et al (1989), Use of difluoromethylornithine in congenital trypanosomiasis at Trypanosoma brucei-gambiense Trypanosoma brucei gambiense]. Tropical Medicine, 39:57–63.

Peacock L et al. (2011), Identification of the meiotic life cycle stage of Trypanosoma brucei in the tsetse fly. Proceedings of the National Academy of Sciences of the United States of America, 108(9):3671–3676.

Picozzi K, Fèvre EM, Odiit M, et al. (2005), Sleeping sickness in Uganda: a thinline two between fatal diseases. BMJ; 331: 1238–41.

Pierre Aubry, Bernard- Alex-Gauzere (2017), Trypanosomiase humaine Africaine ou

maladie du sommeil.

Priotto G et al. (2012), Early prediction of treatment efficacy in second-stage gambiense human African trypanosomiasis. PLoS Neglected Tropical Diseases, 6:e1662.

Priotto G et al.(2009), Nifurtimox-eflornithine combination therapy for second-stage African Trypanosoma brucei gambiense trypanosomiasis: a multicentre, randomised, phase III, non-inferiority trial. Lancet, 374:56–64.

Ruiz JA, Simarro PP (2002), Josendando T. Control ofHAT in the Quicama focus, Angola. Bulletin of the World Health Organization, 80:738–745.

Robays J et al. (2007), Drug toxicity and cost as barriers to community participationin HAT control in the Democratic Republic of Congo,Tropical Medicine and International Health, 12:290–298.

Sullivan L et al. (2013), Proteomic selection of immunodiagnostic antigens for human African trypanosomiasis and generation of a protoype lateral flow immunodiagnostic device.PLoS Neglected Tropical Diseases, 7:e2087.

Simarro PP et al. (2013), Diversity of HAT epidemiological settings requires fine-tunin Control strategiesto facilitate diseaseelimination Research and Reports in Tropical Medicine, 4: 1-6.

Solano P, Jamonneau V, N'Guessan P, et al. (2002), Comparison of different DNA preparation protocols for PCR diagnosis of human trypanosomiasis. Acta Trop, 82: 349-56.

Stanghellini A, Josenando T. (2001), The situation of sleeping sickness in Angola: a calamity. Tropical Medicine and International Health, 6:330–344.

Steverding D. (2008), The history of African trypanosomiasis. Parasites and Vectors, 1:3.

Truc P, Jamonneau V, Cuny G, Frezil JL. (1999), Use of polymerase chain reaction in human African trypanosomiasis stage determination and follow-up. B World Health Org 77: 745–9.

Warren Photographic. (2014), Tsetse Fly (Glossina morsitans) sucking blood from a human arm.

WHO (2009), includes combination of effornithine and nifurtimox in its Essential

List of Medicines for the treatment of human African trypanosomiasis. Population prospects: (2010) the revision /United Nations.