RESEARCH ACTIVITIES CARRIED BY TABORA RESEARCH STATION FOR THE PAST 20 YEARS

National Institute for Medical Research, Tabora Research Station

Background

Tabora Research Station started in 1922 as Sleeping Sickness Service Unit; it was established by Sleeping Sickness Specialist from UK, Dr. F.I. Apted. The Unit was charged with Trypanosomiasis medical surveillance, treatment of sleeping sickness cases and also coordinated treatment, follow-up and liaison with Tsetse control staff.

In 1961 the unit was under the supervision of Dr. Laufer after the retirement of Dr. Apted, by then Dr. Laufer was also Medical Officer Incharge of Tabora. In 1963 the Sleeping Sickness Unit was completely taken over by the Ministry of Health and Dr. R. K. Paul was appointed as Officer Incharge. During that period Tabora was still experiencing catastrophic outbreak of human trypanosomiasis and therefore the Ministry decided to keep Tabora as Sleeping Sickness Co-ordination Unit and main treatment centre of the country.

During that period the control of trypanosomiasis vectors was under the Ministry of Livestock Development (Now Ministry of Agriculture and Livestock Development) whereas the Ministry of Health was charged with the detection and treatment of Human Trypanosomiasis cases. All Sleeping Sickness reports from endemic foci were supposed to be sent to sleeping sickness Unit in Tabora.

Tabora Research Station

According to Tanzania Parliament bill of 1979, which established research institutions, including National Institute for Medical Research Act (1979), Sleeping Sickness Service Unit in Tabora was taken over by the Institute as Tabora Research Station. It was mandated to carry out, co-ordinate, promote, document for research and control of human trypanosomiasis in Tanzania. It is also mandated to formulate priorities for human trypanosomiasis research and control and also monitoring all aspects of sleeping sickness in the country.

In 1989 Dr R K Paul retired and the Late Dr E. K. Komba, Senior Research Scientist was appointed as Head of Station until his sudden demise in 11 November 1996. Currently the Head of Station is Mr S. N. Kibona.

Human Trypanosomiasis Research in Tanzania

Below are research activities carried out by Tabora Research Station for the past 20 years.

1. Clinical Studies

1.1: Presenting Features of Rhodesiense Sleeping Sickness Cases in Kibondo and Kasulu District in Kigoma Region and Tabora. ***(E. Komba and S. Kibona)***

Study on signs and symptoms which may be helpful in aiding diagnosis and /or staging of the disease.

The aim of this study was to look to some of the features of the rhodesiense sleeping sickness which are commonly presented during clinical examination of the sleeping sickness patients, The patients were seen between the period of January - October 1996.

Results

A total of 141 patients was examined in the district hospitals and was asked 12 specific questions from clinical questionnaires in reference to their condition. The most common symptoms expressed were fever, headache, body weakness, cough, back and joint pain and confusion state. These symptoms were found in 80% of the patients. 22.6% had enlarge liver and spleen and 12.7% had oedema.

Duration of illness ranged from one week to 28 weeks, however 78% of the patients reported presence of symptoms for a period of two months or less. An appreciable percentage of primary patients had low haemoglobin level. It was also found that 5 1% of the sleeping sickness patients had evidence of central nervous system involvement, which indicate that many patients go for treatment late.

Many of the signs and symptoms listed for sleeping sickness patients however would be expected to appear in many of the Tropical diseases.

1.2: Clinical Trial of DL-Alpha Difluoromethylornithine (DFMO)/Suramin combination in the treatment of Late Stage Arsenical Refractory Rhodesiense Sleeping Sickness (*E K. Komba*)

This was a collaborative study between NIMR Tabora Station and Kabanga Mission Hospital, Kasulu in Kigoma region. The project was funded by WHO/TDR and started in 1988 to 1992. Only 3 patients were recruited for the study, the recruitment of Melarsoprol refractory patients as required by the first protocol was a drawback since such an occurrence was infrequent. It was therefore WHO/TDR granted a permission to use DFMO/Suramin as first line treatment in which 12 late stage sleeping sickness patients were recruited.

The trial however indicated that this combination of drugs, suramin and Eflornithine (DFMO) is not effective in treatment of late stage rhodesiense sleeping sickness. According to other studies carried out in Gambiense sleeping sickness areas it has shown to be very effective in treating that type of disease.

NB: WHO/TDR and FDA in USA approved the use of DFMO for treatment of Gambiense Sleeping Sickness in 1995.

2. Epidemiology

2.1: Identity of Human-Infective Trypanosomes from Tanzania ***(E. Komba and S. Kibona)***

The study was aimed to investigate and provide a baseline data on trypanosome strain distribution in Tanzania for more extensive future epidemiological studies. The study started by collecting trypanosome stabilates from different foci in Tanzania.

The study was later adopted as *Ph.D.* title, which compared 19 of Tanzanian stocks to determine the Genetic Diversity of *T. b. rhodesiense (Komba et al., 1997).*

In this study it was found that Tanzanian stocks formed a homogeneous group and the predominant genotype isolated in 1991 was still present in the 1994 isolates. The Tanzania stocks were distinct from stocks from other East African foci. This observation does not support the proposal that there are northern and southern strain of *T. b. rhodesiense*, but is consistent with the view that this parasite stocks form a mosaic of different genotypes varying from focus to focus in East Africa.

2.2: Diagnostic Tools

Studies on simple and more effective field diagnostic techniques in human Trypanosomiasis.

2.2.1: Multicentre Evaluation of an Antigen Detection ELISA for the Diagnosis of *T. b. rhodesiense*, Sleeping Sickness. *(E. Komba, S. Kibona and A. K. Ambwene)*

This study was carried in three countries namely, Tanzania, Uganda, and Zambia. The performance of Antigen Detection ELISA was evaluated at four clinical treatment centres, One in Tanzania, Two in Uganda and one in Zambia.

Objective: To Evaluate Antigen Detection ELISA for the Field Diagnosis of Rhodesiense Sleeping Sickness.

Results: The test gave 88 (88.9%) positives out of 99 parasitologically confirmed cases at NIMR Tabora, Tanzania. 99 (94.3%) out of 105 cases tested at the National Sleeping Sickness Control Program (NSSCP), Jinja, Uganda; 86 (87.8%) out of 98 cases tested at the Uganda Trypanosomiasis Research Organisation (UTRO), Tororo, Uganda, and 59 (96.7%) out of 61 cases tested at Tropical Diseases Research Centre (TDRC), Ndola, Zambia.

Overall, the test gave positive results with 332 out of 362 parasitologically proven cases, giving a sensitivity of 92.5%.

There was no cross reactivity with common bacteria], viral or parasitic diseases prevalent in the areas where the studies were conducted, it simple to perform and colour reactions were read visually. This result suggests that Antigen Detection ELISA is potential tool for use in diagnosis of human trypanosomiasis.

2.2.2: Cultivation and In-vitro Cloning of *Trypanosoma rhodesiense* blood stream forms in the absence of feeder layers *(E. Komba)*

(This study was carried out in collaboration with Duke University, USA.)

The major problems in the chemotherapy of sleeping sickness are the toxicity of available drugs and increasing pattern of resistance. This problems call for the development of new drugs in which drug assays are done in in-vitro systems. Previously, in-vitro culture of *Trypanosoma brucei* sub-group involved the use of mammalian cells as a feeder layer. This system had shortcomings like time consuming and very low yielding.

The aim of this study was to provide methods for in-vitro culture of *T. brucei* subgroup in feeder-layer free systems.

By using commercially horse serum, foetal calf serum and goat serum it was demonstrated that the feeder layer systems provide good yield and also provide highly sensitive as well as reproducible technique for assaying trypanocidal drugs. These systems i-nay thus be of potential use for the rapid detecting resistant isolates in the field and clinic.

2.2.3: Multicentre Evaluation of the Card Indirect Agglutination Test for Trypanosomiasis (*Tryp* Tect CIATT®) *(S.N. Kibona and A. K. Ambwene)*

The CIATT was evaluated in four Centres namely, Tanzania and Malawi for *T. b. rhodesiense;* Cote d'Ivoire and Cameroon for *T. ganibiense.*

Objective: To evaluate the use of CIATT for diagnosis of both rhodesiense and gambiense sleeping sickness based on its sensitivity and specificity and to examine its potential in assessing chemotherapeutic cure.

Results: The assay had high relative sensitivity (99.3%) and Specificity (99.4%). Further more, the test gave higher prevalence rates in the general population in endemic foci (27.9% for T *ganibietise* and 21.8% for T *rhodesietise)* compared to the results of parasitological diagnosis (1.4% and 0.7% respectively) (Asonganyi *el al.*, 1998)

In a follow up of antigen positive, parasite negative suspects trypanosomes were detected in 29 (4.2%) suspect seen at the first check up at 3 months- and 17 more cases in suspects seen over 6-18 months. A follow up of patients treated with Melarsoprol revealed that by 9 months post-treatment, 113 (69.0%) of 164 had cleared the antigens from blood circulation, indicating that apart from its diagnostic potential, the assay could be used for evaluating chemotherapeutic cure.

2.2.4: Multicentre Evaluation of Specificity of CTATT in the Field Diagnosis of *T. gambiense and T. rhodesiense* Sleeping Sickness in Non-endemic Areas *(S. Kibona, F. Doua, J. Enyaru, K. Bosonipem)*

This was a study carried out to verify the specificity Tryp Tect CIATT in four centres, Tanzania, Uganda (for *T. rhodesietise),* Cote d'Ivoire and Ghana (for *T. gambiense).*

Objective: To assess the specificity of CIATT in areas, which are non-endemic to sleeping sickness and compare with that of other serological and parasitic methods.

This test was evaluated in a multicentre trial and found to have high relatively sensitivity and specificity (see a. above). Further evaluation of this assay was to be carried out to verify its specificity in areas, which are non- endemic to sleeping sickness. The assay was found to be highly specific in both centres, 99% in

Tanzania, 82% in Uganda, 74% in Ghana and 92% in Cote d'Ivoire.

These results suggest that the assay is a potential tool for diagnosis of sleeping sickness.

3. Research on Malaria

3.1: A study to investigate factors contributing to severe malaria morbidity and consequently mortality in Tabora rural district *(G. Nkya A.K. Ambwene and G.T. Ndamugoba)*

Malaria is a major health problem being ranked number 3 according to out patient and in patient departments records and had the highest case fatality during the same period of December to May in Tabora rural district.

Objectives

1. To determine the proportion of severe malaria morbidity among health service attending patients aiming looking from 1995 up to 1998.
2. To determine malaria related mortality.
3. To determine health seeking behaviour at household level in Tabora rural district.
4. To determine the level of compliance to treatment.
5. To formulate recommendations for implementation to reduce morbidity and mortality due to malaria.

Results

A: Severe Malaria Morbidity

To determine the severe Malaria Morbidity a Retrospective study was conducted. We collected different information from patient records at District hospital/Health Centre. During the study, the sample of 716 malaria cases admitted during 1995-1998 was selected using systematic random sampling. Fever was reported in 89% (637) of the episodes. Severe malaria manifestations were 8% cerebral malaria, 17% Anaemia, in which 6% had Hb levels below 5g/dl. Other symptoms recorded were vomiting dehydration, Drowsiness, unconscious and Jaundice.

Sixteen per cent of the patients with clinical malaria were brought to the Hospital/Health centre the first day of illness and 79% came within 3 days, All cases with significant anaemia came later than 4 days after onset of malaria symptoms.

We believe that the number of clinical episodes of malaria registered at the Hospital/Health centre represents a true picture of malaria morbidity in Tabora Rural district although there may be some under reporting of mild self cured fever cases, especially among the older patients.

The morbidity due to malaria among children was high, especially in the youngest age groups.

B: Complicated Malaria and Mortality

In general, mortality rate appeared to be less than the average for Tanzania (WHO, 1990a). There was 12 mortalities attributed to acute malaria, of which 8 occurred in children below the age of ten. In endemic areas of tropical Africa, morbidity and mortality from Plasmodium falciparum malaria mainly affect children under 5 years of age (Greenwood et at, 1987), In areas of the highest endemicity the incidence of clinical attacks peaks in infants (Binka et at, 1994; Kitua et al. 1996) and severe anaemia is the most frequent life threatening complication.

C: Levels of Compliance and Factors leading to Delayed Treatment Seeking Behavior

To determine Levels of Compliance and Factors leading to delayed treatment-seeking Behavior, questionnaires were administered to 462 households.

In spite of the easy access to medical care in Tabora rural, only 16% of the malaria sick patients (Children & Adults) were brought to the clinic the first day of illness. In that area home treatment either with antimalarials and/or analgesics/antipyretics was very common. Thirty seven percent (37%) (711 out of 462) households reported to use antimalarial drugs before visiting the Hospital/Health centre.

As fever of different origin is common in young children, and is not considered by the villagers as an absolute emergency, it is not surprising that mothers first wait a couple of days to see if the child gets well. However, the will to visit the Hospital/Health centre or clinic appeared to be strong correlated to the distance, i.e. the effort required to reach the clinic. Also it was observed that in Tabora rural, lack of knowledge on malaria case management both by health workers and general population is another big issue. Some of the patients on malaria treatment do not complete the course. That means, it Enhance the drug resistance, complications and death. About 21%(97 out of 462) households reported to delay or to use self-medication because of financial constraints.

Possible Solutions

1. Prompt diagnosis and early treatment of Malaria is the key to prevent severe illness and death.
2. New tools to prevent Malaria Morbidity and Mortality in Tabora rural are needed e.g. Insecticide Treated Bed-Nets (ITN).
3. The Training of Policy Makers, Disease Control Managers and Health Workers, Health Education to clear any misconceptions among the community.

Reference

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