# HUMAN *LOA LOA* (COBBOLD, 1864) (FILAROIDEA: ONCHOCERCIDAE) MORBIDITY DISTRIBUTION IN NORTHERN ENUGU STATE, NIGERIA: IMPLICATIONS FOR ONCHOCERCIASIS CONTROL

**IVOKE, Njoku**
Parasitology and Biomedical Research Unit, Department of Zoology, University of Nigeria, Nsukka, Enugu State, Nigeria. Email: njokuivoke@yahoo.com Phone: 2348039524949.

**ABSTRACT**

***A cross-sectional epidemiological investigation was conducted in Nsukka senatorial zone of Nigeria to evaluate the use of specific clinical signs/symptoms in the assessment of the endemicity, prevalence and morbidity of Loa loa infection in areas meso-endemic for onchocerciasis, and to evaluate the results in respect of the probability of occurrence of adverse reactions, post-treatment with ivermectin in areas presumed to be hypo-, meso-, and hyper endemic for Loa loa infection and morbidity. Standard questionnaire based on the key clinical manifestations of loiasis were administered and the microfilaraemic levels of respondents determined at both community and individual levels. The results showed that the clinical symptoms/signs were known in all the study communities. Altogether 22.0% of respondents (n=1600) positively indicated having experienced either Loa loa infection and/ or Calabar swelling. Based on the questionnaire indices, an intercommunity prevalence of 21.9% (range 17.50 - 27.50%) was established. An overall community median microfilaraemia (mf) prevalence of 19.4% (range 15.0 - 26.3%) was also recorded. A microfilaraemia prevalence >20% was however established in >35% of the study communities indicating the possibility of adverse reaction after ivermectin administration. More males (n=203, 12.7%) than females (n=109, 6.8%) were microfilaraemic. Linear logistic regression indicated that Loa loa infection was significantly associated with age (adjusted odds ratio: 1.12, 95% confidence interval: 1.00-1.14, p<0.001). The intercommunity mean intensity of microfilarial load varied (range 112 ± 25 – 205 ± 30).The best diagnostic performance was obtained for reported history of L. loa with a sensitivity of 100% and a specificity of 94.6%.***

**Keywords:** Epidemiology, Loiasis, Onchocerciasis, Adverse reaction, Microfilaraemia, Implications for Control

## INTRODUCTION

The filarial eye worm *Loa loa*, the aetiologic agent of human loiasis is well known for sometimes migrating across the conjunctiva of the eye, and its association with the transient oedema known as fugitive or Calabar swelling. The parasite which is transmitted to humans through the bite of females of the various species of the tabanid flies of genus *Chrysops* is known to occur in the forested areas stretching from west to central Africa including Benin Republic, Nigeria, Cameroon, Equatorial Guinea, Gabon, Central Africa Republic, Congo Democratic Republic, Republic of Congo and Sudan. For long, loiasis has been regarded as a benign form of filariasis and consequently has been little studied (Gordon *et al*., 1950; Kershaw, 1951). The current resurgence of interest in *L. loa* and its associated morbidity has been attributed to a number of factors including firstly, the disease being one of the primary causes ( after malaria and respiratory infections) of medical consultation in endemic areas (Pinder, 1988). Secondly, it has been found that the filaricidal drug, ivermectin (Mectizan®), administered as a single dose brings about dramatic decrease in the microfilaraemia load and an improvement in some clinical signs related to the disease. (Carme *et al*., 1991; Hovette *et al*., 1994; Gardon *et al*., 1997b). Thirdly, in some areas where loiasis and onchocerciasis are co-endemic, community-directed treatment of onchocerciasis with ivermectin (CDTI) and hence onchocerciasis control, had virtually come to a standstill because of the risk of severe adverse reactions. The reactions occur in individuals heavily infected with *Loa loa* and include potentially degenerative effects in the brain (Gardon *et al*., 1997a; Twum-Danso, 2003). Systemic infections affecting other organs such as the heart and kidney have also been reported (Carme *et al*., 1991; Chippaux *et al.,* 1996; Gardon *et al.,* 1997a; Boussinesq *et al.,* 1998). The third factor becomes very poignant in view of the on-going ivermectin distribution programme against onchocerciasis in some African countries including many in areas where *L. loa* is co-endemic with *Onchocerca volvulus* infection.

Available data indicate that such areas at risk of ivermectin-induced severe adverse reactions appear to be restricted to the forested parts of Cross River, Abia, Imo, and Delta States of Nigeria. Also in Nigeria, the most loiasis-affected areas are south of latitudes 6º N, that is, the area around the Niger delta and between the delta and the boundary between Nigeria and Cameroon. At Sapelle, Kershaw (1955) recorded 22.2 % loiasis prevalence in the population while Duke and Moore (1961) reported reduced loiasis prevalence of 12.9% in the same area. Udonsi (1986) and Arene and Atu (1986) studied the endemicity of loiasis in the eastern parts of the Niger delta. In the south-eastern part of Nigeria, Emeribe and Chuks-Ejezie (1989) found a prevalence of 1.3% among blood donors in Calabar

municipality. In the south-west of Nigeria, epidemiological studies were conducted by Akinboye and Ogunrinade (1987) and earlier by Ogunba (1977). North of latitude 8º N, Ufomadu *et al.* (1991) conducted loiasis surveys in Plateau State while Akogun (1992) examined villagers in the then Gongola State where a 0.9% prevalence was recorded. Enugu State has been reported to be mesoendemic for onchocerciasis in areas potentially endemic for *L loa* (Nwaorgu *et al.,* 1994; Ivoke 2004). While it is not feasible to determine the intensity of loiasis infection for all individuals living in areas targeted for ivermetin treatment which may also be co-endemic for *L. loa*, Noireau *et al*. (1990) had suggested the usefulness of specific clinical manifestations to assess *L. loa* at the individual and community levels. An epidemiologic method that can be used to rapidly assess communities at risk of developing severe adverse reactions post-ivermectin treatment for onchocerciasis due to co-infection with *L. loa* was substantiated and validated in a WHO/TDR (2001) multi-country study using both parasitological and questionnaire methods.

The main objective of this study was to conduct a cross-sectional survey of the distribution of *L. loa* infection and disease at Nsukka area in order to identify communities where large scale distribution of ivermectin for onchocerciasis control should be programmed to incorporate careful monitoring of individuals to prevent the possible risk of occurrence of *L. loa*-induced post ivermectin treatment adverse reaction. Secondly, the study aimed also at investigating the relationship between the parasitological prevalence and the rapid assessment indices based on the clinical manifestations of *L. loa* morbidity. The implications of the study to the on-going onchocerciasis control program were also discussed.

## MATERIALS AND METHODS

**The Study Area**: The study area consists of twenty (20) randomly selected communities from Nsukka, Udenu, Igbo Eze North, Igbo Eze South, Uzo Uwani, Igbo Etiti and Isi Uzo Local Government Areas (LGAs) all within Nsukka senatorial zone of Enugu State , Nigeria . The area lies between latitudes 6º 40' N to 7º 00' N and longitudes 7º 00' E to 7º 32' E with an estimated total population of 125,245 based on the 1991 Nigeria national population census figures and a WHO annual population growth projection of 2 ½ % . The entire study area is ecologically homogenous with the vegetation consisting of the guinea-savannah mosaic type with its characteristic grass-topped hills and dry valleys. For much of the year, the area experiences high temperatures (25ºC-30ºC) with two distinct seasons; - a rainy season of 7 months from April to October and a shorter dry season of 5 months from November to March. The annual precipitation is between 1200-3000 mm. Rivers are few but they are natural springs which serve as all-season sources of water. Subsistence agriculture and trading are the dominant occupations of the inhabitants with potatoes, yam, rice, maize, cassava, bananas, palm oil, groundnuts, pepper, citrus fruits, as the major crops (Ofomata, 1979).

**Study Population and Data Collection:** Administrative clearance was obtained in advance of the survey from the various local government administration offices. Health officials at the local government levels were also contacted and briefed on the objectives and expected outcome of the study.

Preliminary visits were made to the study communities to inform the villagers about the rationale of the study and to obtain their collective consent, and for the community leaders to mobilize their respective respondents before the arrival of the study group. Also during the preliminary trips, the community-level questionnaire eliciting information on the knowledge and local names of *L. loa* infection were administered to the village heads.

Based on reports of a pilot assessment of potentially *L. loa* endemic areas, 20 study communities were randomly selected in the zones earmarked for inclusion in ivermectin treatment campaigns for onchocerciasis. Assessment of the *L. Loa* endemicity at community level was done by the use of standardized questionnaire (based on the clinical signs of loiasis). For individual questionnaires, 80 individuals were randomly selected from each of 20 communities thus providing a sample size of 1600. Households were randomly selected and in each selected household all individuals aged ≥ 15 years and who had been resident in the community for at least 5 years, and who consented to participate, were included in the study. Individuals aged ≥ 15 years were selected because the initial reports of severe adverse reaction occurred in persons aged $\underline{>}$ 15 years (Boussinesq *et al.,* 1998).

Interview of eligible individuals in each household was conducted after explaining the objectives of the study and obtaining informed consent. Respondents were interviewed one at a time to ensure confidentiality and to avoid influencing the responses of other members of the household. The questions administered sequentially to each respondent are as follows:

a. Have you ever experienced or noticed worms moving along the white part of your eye?
b. Have you ever had the condition in this picture? ( interviewee is guided to recognize a photograph of *L. loa* across the conjunctiva)
c. Have you ever experienced swellings under the skin that change position or disappear?
d. For how long did the swelling last?

**Parasitological Examination:** After informed consent, each respondent interviewed underwent a parasitological examination to determine the prevalence and intensity of *L. loa* infection. Blood samples (50 ml) were collected from each respondent by the nurses allocated to us by the senior medical officers in-charge of the general hospitals at Nsukka and Ogrute. Blood samples were obtained by the finger-prick method as described previously (Ivoke,

2000). The blood obtained between 1000 h and 1600 h was used to determine the intensity of microfilaraemia by preparing thick blood smear on an area (1.5 cm × 2.5 cm) of a grease-free glass slide. The smear was dried, dehaemoglobinized, using tap water for 5-10 minutes, dried again, fixed with methyl alcohol (1 minute), stained in Giemsa buffered with 8% phosphate (pH 7.2 ) and allowed to dry. The *L. loa* microfilariae were identified at ×40 magnification using the method of Ash and Orihel (1997). Counting the microfilariae was carried out using the technique of Denham *et al.* (1971)

**Data Analysis:** All data derived from the questionnaires and parasitological procedures were entered and analysed. Logistic regression analysis was performed to assess the most reliable reported symptoms/signs for predicting individual *L. loa* infection at 95 % confidence interval and to evaluate the association between *L. loa* infection and the best performing reported symptom. The prevalence of loiasis based on the questionnaires and parasitological methods were determined and their relationships evaluated. The intensity of mf was expressed as number of microfilariae per millilitre (mf/ml) of blood on individual level. At the community level the intensity of *L. loa* infection was expressed as mean microfilariae per millilitre (mf/ml) of blood. Based on the prevalence of microfilariae in the study group aged ≥ 15 years the study population was subsequently categorized according to the following age classes: 15 — 19, 20 — 29, 30 — 39, 40 — 49, 50 — 59 and ≥ 60.

The study communities were further classified, as follows into 3 endemic levels, as a proxy for transmission intensity; low endemicity (≤ 25 % mf prevalence), moderate endemicity (25 — 34.9% mf prevalence), and high endemicity (≥ 35 % mf prevalence).

Diagnostic performance of the questionnaires for identifying at-risk communities for adverse reaction post-ivermectin treatment for onchocerciasis was obtained by calculating the sensitivity, specificity, and predictive values including 95% confidence intervals. A threshold of 40 % prevalence of *L. loa* infection and 20 % microfilaraemia were used based on WHO/TDR (2001) recommendations.

## RESULTS

A total of 20 communities were surveyed and 1600 respondents consisting of 785 (49.1 %) males and 815 (50.9 %) females were interviewed using *Loa loa* endemicity/morbidity assessment indices. *L. loa* (eye worm) was well known in all the study communities and had similar local terms in the linguistically homogeneous study area. The terminology for *L. loa* as used in all the study localities was descriptive of the appearance of the parasite across the conjunctiva, hence the local term "ari anya" meaning "worm of the eye".

Based on the questionnaire indices, 352 (22.0%) respondents of the study population (n=1600) positively indicated having experienced either history of the eye worm and/or the transient oedema (Calabar swelling) (Table 1). The between-community median age of the interviewees varied considerably from 24 to 36 years while the intra-community age also varied widely from 20-38 years in Abbi community to 15-56 years in Orba (Table 1). The overall between-community prevalence range was 17.5-27.5% while the overall median *L. loa* infection prevalence was 21.9%.

Specifically 248 (15.5%) respondents composed of 149 (9.3%) males and 99 (6.2%) females indicated having experienced the eye worm (confirmed by showing the interviewee a black and white photograph of the parasite across the conjunctiva). Only 104 (6.5%) of total respondents composed of 62(3.9%) males and 42(2.6%) females indicated having experienced Calabar swelling. Between-sex difference was not statistically significant ($p>0.05$). Most of the study communities had no local terms for Calabar swelling and the most commonly cited location for the swelling was, in sequence, upper extremities, lower extremities, the whole body. Calabar swelling appears less specific for the perception of *L. loa* infection and morbidity than the reported history of the eye worm. The age and sex distribution of *L. loa* microfilaraemia among the study population in the different communities is shown in Table 2. An overall microfilaraemia of 19.5% involving 312 microfilaraemia-positive respondents (203 males and 109 females) was established. The community median microfilaraemia prevalence of 19.4% was also recorded. The community microfilaraemia prevalence varied considerably (range 15.0-26.3%). The lowest prevalence was recorded for Nsukka urban and Opi where 12(15.0%) of respondents from each of the localities tested microfilaraemic. Further away from the urban setting, the prevalence of the microfilaraemia appeared to be much higher, ranging from 20.0% at Amaeze, Iheakpu, and Orba to 26.3 % at Owerre Eze-Orba. The results further indicate that 7(35 %) of the total study communities (n=20) fulfilled the parasitological threshold definition of high-risk communities (≥ 20% microfilaraemia prevalence) for adverse reaction post-ivermectin treatment. Other communities (n=13), (65.0 %) recorded microfilaraemia prevalence < 20% implying that community-directed ivermectin distribution could be conducted with considerable safety. Generally 18 (90.0%) of the study communities were of low *L. loa* microfilaria endemicity (≤ 25.0% mf prevalence) while 2 communities (10.0 %) of study localities were of moderate *L. loa* endemicity (25.0 - 34.9 % mf prevalence).

*Loa loa* microfilaraemia affected, to varying degrees, respondents of all the 6 age categories and appears to increase with age, peaking at the 30-39 years age range. Respondents (n=284) aged 15 - 49 years showed higher *L. loa* microfilaraemia rate (91.0 %) than those aged ≥ 50 years (n=28) that indicated a microfilaraemia rate of 9.0 %. Linear logistic regression indicated that an infection with *L. loa* was significantly associated with age (adjusted odds ratio:

**Table 1: Locality, Gender and Age-distribution of Respondents to Questionnaires in *Loa loa* Endemic Communities of Northern Enugu State, Nigeria**

| Community | No. interviewed | | | Median age (range) | Assessment Indicators | | | | | | Community | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Positive history eye worm | | | Calabar Swelling | | | Total | Prevalence |
| | M | F | Total | | M | F | Total | M | F | Total | | % |
| **Obukpa** | 30 | 50 | 80 | 29(16-45) | 11 | 5 | 16 | 3 | 1 | 4 | 20 | 25.00 |
| **Iheakpu** | 42 | 38 | 80 | 33(18-50) | 7 | 4 | 11 | 3 | 5 | 8 | 19 | 23.75 |
| **Abbi** | 35 | 45 | 80 | 24(20-38) | 6 | 7 | 13 | 4 | 0 | 4 | 17 | 21.25 |
| **Adani** | 47 | 33 | 80 | 34(16-50) | 7 | 9 | 16 | 3 | 3 | 6 | 22 | 27.50 |
| **Ibeagwa** | 41 | 39 | 80 | 30(15-45) | 4 | 6 | 10 | 4 | 1 | 5 | 15 | 18.75 |
| **EnuguEzike** | 34 | 46 | 80 | 26(16-35) | 10 | 2 | 12 | 1 | 2 | 3 | 15 | 18.75 |
| **Ovoko** | 46 | 34 | 80 | 31(17-45) | 4 | 5 | 9 | 3 | 4 | 7 | 16 | 20.00 |
| **Ede Oballa** | 36 | 44 | 80 | 28(15-38) | 9 | 6 | 15 | 2 | 2 | 4 | 19 | 23.75 |
| **Nsukka urban** | 38 | 42 | 80 | 24(18-35) | 6 | 4 | 10 | 4 | 1 | 5 | 15 | 18.75 |
| **Ehalumona** | 43 | 37 | 80 | 35(15-55) | 8 | 5 | 13 | 1 | 3 | 4 | 17 | 21.25 |
| **Opi** | 28 | 52 | 80 | 32(15-40) | 5 | 6 | 11 | 3 | 0 | 3 | 14 | 17.50 |
| **Uzo Uwani** | 50 | 30 | 80 | 28(16-37) | 11 | 5 | 16 | 3 | 1 | 4 | 20 | 25.00 |
| **Amaeze** | 41 | 39 | 80 | 30(16-48) | 7 | 3 | 10 | 4 | 4 | 8 | 18 | 22.50 |
| **Aku** | 45 | 35 | 80 | 28(18-47) | 6 | 7 | 13 | 2 | 1 | 3 | 16 | 20.00 |
| **Obimo** | 39 | 41 | 80 | 24(19-33) | 8 | 4 | 12 | 4 | 2 | 6 | 18 | 22.50 |
| **Orba** | 42 | 38 | 80 | 35(15-56) | 10 | 2 | 12 | 4 | 1 | 5 | 17 | 21.25 |
| **Nuru** | 33 | 47 | 80 | 30(17-42) | 5 | 6 | 11 | 2 | 2 | 4 | 15 | 18.75 |
| **Obollo Afor** | 44 | 36 | 80 | 27(15-46) | 7 | 4 | 11 | 5 | 3 | 8 | 19 | 23.75 |
| **Owerre Ezeoba** | 38 | 42 | 80 | 36(16-50) | 8 | 5 | 13 | 4 | 5 | 9 | 22 | 27.50 |
| **Echara** | 33 | 47 | 80 | 35(19-46) | 10 | 4 | 14 | 3 | 1 | 4 | 18 | 22.50 |
| **Total** | 748 | 815 | 1600 | | 149 (9.3%) | 99 (6.19%) | 248 (15.5%) | 62 (3.88%) | 42 (2.63%) | 104 (6.5%) | 352 | 22.000 |

*Key: M= Male; F= Female*

**Table 2: Age and Sex-Specific distribution of *Loa loa* Microfilaraemia among Inhabitants of Selected Communities in Northern Enugu State, Nigeria**

| Community | No examined | Age – group (yrs) | | | | | | | | | | | | No. mf +ve | Prevalence |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 15 - 19 | | 20 - 29 | | 30 - 39 | | 40 - 49 | | 50 - 59 | | ≥60 | | | % |
| | | M | F | M | F | M | F | M | F | M | F | M | F | | |
| **Obukpa** | 80 | 3 | 1 | 4 | 2 | 2 | 3 | 2 | 1 | 0 | 0 | 0 | 0 | 18 | 22.5 |
| **Iheakpu** | 80 | 2 | 1 | 1 | 3 | 4 | 1 | 1 | 2 | 1 | 0 | 0 | 0 | 16 | 20.0 |
| **Abbi** | 80 | 3 | 3 | 2 | 3 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 15 | 18.8 |
| **Adani** | 80 | 2 | 2 | 4 | 0 | 2 | 2 | 3 | 1 | 2 | 0 | 2 | 0 | 20 | 25.0 |
| **Ibeagwa** | 80 | 2 | 0 | 2 | 2 | 3 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 13 | 16.3 |
| **EnuguEzike** | 80 | 2 | 2 | 3 | 1 | 2 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 13 | 16.3 |
| **Ovoko** | 80 | 3 | 0 | 2 | 2 | 2 | 2 | 1 | 2 | 0 | 0 | 0 | 0 | 14 | 17.5 |
| **Ede Oballa** | 80 | 4 | 0 | 3 | 2 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 13 | 16.3 |
| **Nsukka Urban** | 80 | 2 | 2 | 3 | 1 | 1 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 12 | 15.0 |
| **Ehalumona** | 80 | 2 | 1 | 1 | 2 | 2 | 0 | 2 | 2 | 2 | 0 | 0 | 0 | 14 | 17.5 |
| **Opi** | 80 | 1 | 1 | 2 | 1 | 3 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 12 | 15.0 |
| **Uzo Uwani** | 80 | 2 | 2 | 3 | 0 | 2 | 1 | 2 | 2 | 3 | 1 | 0 | 0 | 18 | 22.5 |
| **Amaeze** | 80 | 4 | 1 | 2 | 2 | 3 | 1 | 3 | 0 | 0 | 0 | 0 | 0 | 16 | 20.0 |
| **Aku** | 80 | 1 | 2 | 1 | 2 | 3 | 0 | 1 | 2 | 2 | 0 | 0 | 0 | 14 | 17.5 |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Obimo** | 80 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 0 | 17 | 21.3 |
| **Orba** | 80 | 2 | 1 | 0 | 3 | 2 | 1 | 3 | 0 | 3 | 1 | 0 | 0 | 16 | 20.0 |
| **Nguru** | 80 | 3 | 1 | 2 | 0 | 3 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 14 | 17.5 |
| **Obollo Afor** | 80 | 2 | 2 | 3 | 1 | 1 | 3 | 2 | 2 | 1 | 1 | 0 | 0 | 18 | 22.5 |
| **Owerre Ezeoba** | 80 | 3 | 2 | 4 | 0 | 3 | 2 | 3 | 0 | 4 | 0 | 0 | 0 | 21 | 26.3 |
| **Echara** | 80 | 3 | 1 | 2 | 2 | 3 | 1 | 4 | 0 | 2 | 0 | 0 | 0 | 18 | 22.5 |
| **Total (%)** | 1600 | 48 (3.0) | 27(1.7) | 46 (2.9) | 30(1.9) | 50 (3.1) | 30(1.9) | 35 (2.2) | 18(1.1) | 21(1.3) | 4(0.3) | 3 (0.2) | 0(0.0) | 312 (19.5) | 19.5 |

**Table 3: Distribution of *Loa loa* Microfilaraemia and Mean Intensities of the Individual and Community Microfilarial Loads among Microfilariae – Positive Respondents**

| Community | No. Blood smear examined | No. mf +ve ( % ) | Mean intensities ± SE | Median intensity | Range (mf/ml) |
|---|---|---|---|---|---|
| **Obukpa** | 80 | 18 | 210 ± 56 | 148 | (22 -306 ) |
| **Iheakpu** | 80 | 16 | 205 ± 25 | 95 | ( 40 -292 ) |
| **Abbi** | 80 | 15 | 120 ± 38 | 82 | ( 27 – 251 ) |
| **Adani** | 80 | 20 | 125 ± 27 | 58 | (39 – 273 ) |
| **Ibagwa** | 80 | 13 | 200 ± 24 | 167 | (32 – 303 ) |
| **Enugu Ezike** | 80 | 13 | 160 ± 35 | 112 | ( 49 – 224 ) |
| **Ovoko** | 80 | 14 | 185 ± 25 | 145 | ( 36 – 241 ) |
| **Ede Oballa** | 80 | 13 | 190 ± 30 | 158 | (62 – 210 ) |
| **Nsukka Urban** | 80 | 12 | 185 ± 27 | 174 | ( 50 – 198 ) |
| **Ehalumona** | 80 | 14 | 210 ± 39 | 196 | (26 – 233 ) |
| **Opi** | 80 | 12 | 118 ± 32 | 88 | ( 42 – 164 ) |
| **Uzo Uwani** | 80 | 18 | 215 ± 14 | 175 | ( 67 – 225 ) |
| **Amaeze** | 80 | 16 | 112 ± 25 | 96 | ( 38 – 182 ) |
| **Aku** | 80 | 14 | 145 ± 36 | 68 | ( 24 – 225 ) |
| **Obimo** | 80 | 17 | 170 ± 40 | 111 | ( 57 – 196 ) |
| **Orba** | 80 | 16 | 235 ± 30 | 176 | ( 42 – 244 ) |
| **Nguru** | 80 | 14 | 210 ± 24 | 242 | ( 22 – 249 ) |
| **Obollo Afor** | 80 | 18 | 205 ± 30 | 182 | ( 86 – 232 ) |
| **Owerre Ezeoba** | 80 | 21 | 195 ± 27 | 104 | ( 30 – 210 ) |
| **Echara** | 80 | 18 | 213 ± 33 | 160 | (22 – 243 ) |
| **Total** | 1600 | 312 | 52±15 | 213 | 122-306 |

**Table 4: Diagnostic Performance of Assessment Indices as Predictors of *Loa loa* Microfilariae – High Risk Communities**

| Questionnaire assessment indices | Interview threshold of high risk | Diagnostic Performance | | | |
|---|---|---|---|---|---|
| | | Sensitivity % | Specificity % (range) | Positive predictive value % (range) | Negative predictive value % |
| **History of eyeworm** | >40% *L. loa* prev. > 20% | 100 | 62.8 ( 47. 8 – 71.6 ) | 55.7 (38.8 – 66.3) | 100 |
| **History of eyeworm plus photograph of worm across eyeball** | >40% *L. loa* prev. >20% | 100 | 94.6 ( 63.7 – 98.8 ) | 82.2 ( 53.2 -91.0 ) | 100 |
| **History of Calabar swelling** | >40% *L. loa* prev. >20% | 80 | 55.0 (38.8 – 71.4 ) | 53.5 (41.1 – 63.7 ) | 100 |
| **History of Calabar swelling of 7 days duration** | >40% *L. loa* prev. >20% | 90.3 | 75.7 ( 49.3 – 89.2 ) | 71.0 (56.2 – 83.4 ) | 92.4 |

***Key:*** *prev. = prevalence; figures in parentheses are 95% confidence intervals*

**Table 5: Assessment of some Confounding Factors for Predicting *Loa loa* Infection**

| Variable | Adjusted Odds ratio | P-value |
|---|---|---|
| **Reported history of eye worm** | 1.48 (1.32 – 1.68 ) | <0.001 |
| **Reported history of Calabar swelling** | 1.34 ( 1.12 – 1.55 ) | <0.001 |
| **Sensitivity to light** | 0.95 ( 0.64 – 1.17 ) | 0.078 |
| **Nausea** | 0.69 (0.53 – 0.98 ) | 0.037 |

*Figures in parentheses are 95% confidence intervals.*

1.12, 95% confidence interval: 1.00 - 1.14, p < 0.001). No such association was found for sex (adjusted odds ratio: 0.04, 95 %) confidence interval: 0.03-0.09, p < 0.01) although more males (n = 203, 12.7 %) than females (n = 109, 6.8 %) were microfilaraemic from the population.

Table 3 shows the distribution of *L. loa* microfilaraemic individuals and the mean intensity of the positive microfilarial loads for each of the 20 study communities. The inter-community mean intensity of microfilarial load varied from one community to another (range 112 ± 25 — 235 ± 30). Among the mf – positive respondents at Nsukka and Obollo – Afor, mean mf – intensities of 185 ± 27 and 205 ± 30 were recorded respectively._Although wide variations in the mean mf intensities were recorded generally (range 58 mf/ml – 182 mf/ml), the inter–community mean mf intensity difference was not statistically significant (p > 0.05). The diagnostic performance of the *L. loa* assessment indicators is shown in Table 4. All the assessment indices showed good sensitivity (the probability that a truly *L. loa* microfilaraemic individual will test positive (range 80.0% – 100%), and specificity, (the probability that a truly uninfected individual will test negative (amicrofilaraemic), (range 55.0% – 94.6%), and specificity. Reported history of the transient Calabar swelling was relatively low at 55.0% (range 38.8% - 71.4%). The best diagnostic performance was obtained for the reported history of eye worm confirmed with the photograph of *L. loa* across the conjunctiva which had a sensitivity of 100% and a specificity of 94.6% (range 63.7% – 98.8%). Comparisons between the interviewees" responses and their *L. loa* infection levels further revealed that the reported history of Calabar swelling of 7 days duration was a better predictor of *L. loa* infection (sensitivity, 90.3%; specificity, 75.7%) than the reported history of Calabar swelling alone.

The results indicate that the assessment indices based on simple questionnaires could be used to predict *L. loa* parasitological prevalence, and hence the risk of severe adverse reactions associated with ivermectin treatment in onchocerciasis control programme. The result further indicates that individuals infected with *L. loa* more often reported *L. loa* migration across the conjunctiva.

The result of the logistic analysis, carried out at the individual level to assess potential predictors of the association between *L. loa* infection and the reported symptoms is shown in Table 5. Reported history of eye worm and transient oedema of 7 days duration were identified as the symptoms/signs with the strongest association with *L. loa* infection at the individual level with adjusted odds ratios respectively as 1.48 ( 95% confidence interval: 1.32 – 1.68, p < 0.001 ) and 1.34 ( 95% confidence interval: 1.12 – 1.55, p < 0.001 ). No significant odds ratios were found between *L. loa* infection and sensitivity to light or nausea.

## DISCUSSION

Although it has been established by earlier surveys that the most *Loa loa* endemic communities in Nigeria are located south of latitude 6ºN (Udonsi,1986; Arene and Atu, 1986), the present study further indicated that the disease was well known in the ecologically homogenous communities of the guinea-savannah belt north of latitude 6ºN. The result therefore confirmed earlier reports (Ufomadu *et al.,* 1991; Akogun, 1992).

The results obtained based on the questionnaire determinants of *L. loa* infection and morbidity indicate that while most of the study communities had no local terminologies for the transient *L. loa*-induced Calabar swelling, a substantial number 104 (6.5%) of the respondents (n= 352) positively indicated having experienced the oedema while 248 (15.5%) had actually reportedly experienced the infection The result further showed not only that loiasis is endemic in the study communities but also established a total prevalence of 22.0% (Table 1). The prevalence obtained was considerably lower than the WHO-recommended ≥40% threshold for identifying communities at high risk of *L. loa*-induced adverse reactions post-ivermectin treatment, indicating that, based on the questionnaire indices, ivermectin distribution for onchocerciasis control programme may be safely conducted in the study communities. The result indicates too that questionnaire predictors could be employed as useful tools in the rapid assessment of *L. loa* infection.

*Loa loa* microfilaraemia affected, to varying degrees, respondents of the different ages within the scope of study and appeared to be age-dependent (Table 2). Thus, respondents aged 15 – 49 years showed higher *L. loa* microfilaraemia rate (91.0%) than individuals aged ≥50 years. The result was further validated by logistic regression indicating the infection with *L. loa* was significantly associated with age (adjusted odds ratio; 1.12, 95% confidence interval: 1.00 – 1.14, p < 0.001). The age-dependent feature of the infection may be attributed to the degree of exposure to the bites of the haematophagous female tabanid vectors by the active segment of the population in endemic communities with the risk of exposure decreasing with age as more protective clothing are worn by the less active-aged individuals.

The overall microfilaraemia prevalence of 19.5% established differs from the result obtained in the selected villages of Cross River State where prevalence ranging from 0-1.7% (median prevalence 1.5%) were obtained (WHO/TDR, 2001).

The mean intensity of the community microfilaria loads showed much variation (range 112 ± 25—235 ± 30) with the urban and semi- urban centres recording low mean microfilarial intensities among the mf-positive respondents (Table 3).

Although wide variations of the mean and median community microfilaria intensities were prevalent in the rural community setting (range 58 mf/ml—182 mf/ml) of blood, the individual microfilaria load was very low (5.24±15 mf/ml) and substantially less then the 8000 mf/ml threshold above which severe adverse reactions may be anticipated. The result corroborates that obtained using the questionnaire indicators and implies that severe adverse reactions may not occur in individuals in any of the study communities.

The diagnostic performance of the questionnaire indices (Table 4) indicates that all the factors showed good sensitivity and specificity, while the negative predictive values were generally high. These high negative predictive values could be attributed to the absence of other confounding factors in the *L. loa* microenvironment. The overall performance of the questionnaire indices appears to provide a positive indication that the simple questionnaires could be used as determinants of *L. loa* prevalence in endemic communities. At the individual level, symptoms and/or signs with the strongest association with loiasis morbidity were the reported history of the eye worm followed by the history of the transient Calabar swelling. The result is in conformity with those of a multi-country study in which *L. loa* infection and morbidity were associated with oedema lasting for 7 days (WHO/TDR, 2001).

**Implications for Onchocerciasis Control:** Good quality diagnostic tests that are fit and provide accurate results are of paramount importance in reducing the burden of infectious diseases. The lack of access to good quality diagnostic tests for infectious diseases contributes to the enormous burden of ill health globally. Recent technological developments have led to the proliferation of new rapid diagnostic tests that hold promise for the improved management and control of infectious diseases. A confident diagnosis can sometimes be made on the basis of clinical signs or symptoms. In settings where access to diagnostic laboratory services is limited, the use of questionnaire tools has been in practice.

In loiasis many individuals do not present with microfilariae in their peripheral blood yet may prove to be infected because of previous history of subconjuctiva worm passage.

The use of questionnaire to screen communities at high risks of *L.loa* microfilaraemia and morbidity and subsequently to identify areas where serious adverse reactions may occur post-ivermectin treatment for onchocerciasis control has been highlighted in this study. The use of standard questionnaires have been successfully employed in parts of Africa to screen for infections due to *Schistosoma haematobium* with diagnosis at the community level as the main objective (Langeler *et al*., 1991; Ekwunife and Okafor, 2005). The use of questionnaire is therefore a promising alternative to the current invasive, and time-consuming parasitological methods. The methodology appears faster, less expensive and can be easily adapted for use in rural settings where efficient and adequate conventional parasitological diagnosis may not be readily available. The onchocerciasis control programme will get a boost in coverage.

**ACKNOWLEDGEMENTS**

I am grateful for the participation of Ms Tochukwu Ogbaje of Department of Zoology, University of Nigeria, and the medical auxiliaries from the General hospitals at Enugu Ezike and Nsukka, for assistance in the field work and data collection. My gratitude extends to all the respondents and civic leaders for their invaluable cooperation.

**REFERENCES**

AKINBOYE, D. O. and OGUNRINADE, A. F. (1987). Malaria and loiasis among blood donors at Ibadan, Nigeria. *Transactions of the Royal Society of Tropical Medicine and Hygiene, 81*: 398 – 399.

AKOGUN, O. B. (1992). Filariasis in Gongola State, Nigeria .I. Clinical and parasitological studies in the Mutum – Biyu district. *Angewandte Parasitologie, 33:* 125 – 131.

ARENE, F. O. and ATU, F. N. (1986). *Mansonella perstans* microfilaraemia among the Bori community of the Niger Delta area of Nigeria. *Annals of Tropical Medicine and Parasitology, 89:* 535 – 536.

ASH, L. R. and ORIHEL, T. C. (1997). *Atlas of Human Parasitology.* (4th ed). American Society of Clinical Pathologists. Chicago.

BOUSSINESQ, M., GARDON, J., GARDON–WENDEL, N., KAMGNO, J., NGOUMOU, P. and CHIPPAUX, J. P. (1998). Three probable cases of *Loa loa* encephalopathy following ivermectin treatment for onchocerciasis. *American Journal of Tropical Medicine and Hygiene, 58(4):* 461 -469.

BOUSSINESQ, M., GARDON, J. and PION, S. D. S. (2001). Relationship between the prevalence and intensity of *Loa loa* infection in the Central Province of Cameroon. *Annals of Tropical Medicine and Parasitology, 95(5):* 495 – 507.

CARME, B., BOULESTEIX, J., BOUTES, H. and PURUEHNCE, M. F. (1991). Five cases of encephalitis during treatment of loiasis with diethylcarbamazine. *American Journal of Tropical Medicine and Hygiene, 44:* 684 – 690.

CHIPPAUX, J. P., BOUSSINESQ. M., GARDON, J., GARDON-WENDEL, N. and ERNOULD, J. C. (1996). Severe adverse reaction risk during mass treatment with ivermectin in loiasis-endemic areas. *Parasitology Today, 12:* 448 – 450.

DENHAM, D. A., DENNIS, D. T., PANNUDURAI, T., NELSON, G. S. and GUY, F. (1971). Comparison of counting chamber and thick smear methods of counting microfilariae. *Transactions of the Royal Society of Tropical Medicine and Hygiene, 65:* 521 – 525.

DUKE, B. O. L. and MOORE, J. P. (1961). A trial of banocide as a means of controlling the transmission of loiasis on a rubber estate in Nigeria., *Annals of Tropical Medicine and Parasitology, 55:* 263 – 267.

EKWUNIFE, C. A. and OKAFOR, F. C. (2005). Questionnaire as a tool for identification of high risk communities in urinary schistosomiasis research. *Animal Research International, 2(2): 287 – 291.*

EMERIBE, A. O. and CHUKS-EJEZIE, G. (1989). Haemoparasites of blood donors in Calabar. *Tropical Geographical Medicine, 41*: 61 – 65.

GARDON, J., GARDON-WENDEL, N., DEMANGA-NGANGUE, KAMGNO, J., CHIPPAUX, J. P. and BOUSSINESQ, M. (1997a). Serious reactions after mass treatment of onchocerciasis with ivermectin in an endemic area for *Loa loa* infection. *Lancet, 350*: 18 -22.

GARDON, J., KAMGNO, J., FOLEFACK, G., GARDON-WENDEL, N., BOUCHITE, B. and BOUSSINESQ, M. (1997b). Marked decrease in *Loa loa* microfilaraemia 6 and 12 months after a single dose of ivermectin. *Transactions of the Royal Society of Tropical Medicine and Hygiene, 91*: 593 – 594.

GORDON, R. M., KERSHAW, W. F., CREWE, E. and OLDROYD, H. (1950). The problem of loiasis in Africa with special reference to recent investigations at Kumba in the British Cameroon and Sapelle in Southern Nigeria. *Transactions of the Royal Society of Tropical Medicine and Hygiene, 44:*11 – 41.

HOVETTE, P., DEBONNE, J. M., TOUZE, J. E., GAXOTTE, P., IMBERT, P., FOURCADE, L., and LAROCH, R. (1994). Efficacy of ivermectin treatment of *Loa loa* filariasis patients without microfilaraemia. *Annals of Tropical Medicine and Parasitology, 88*: 93 - 94.

IVOKE, N. (2000). Rural bancroftian filariasis in north-western Cameroon: Parasitological and clinical studies*. Journal of Communicable Diseases, 34(4):* 254-263.

IVOKE, N. (2004). An epidemio-dermatological assessment of onchocercal skin diseases in Awhum, Enugu State, Nigeria. *Bio-Research, 2(2)*: 46 – 53.

KERSHAW, W. E. (1951). Studies on the epidemiology of filariasis in West Africa, with special reference to the British Cameroons and the Niger Delta 11. The influence of town and village evolution and development on the incidence of infections with *Loa loa* and *Acanthocheilonema pertans*. *Annals of Tropical Medicine and Parasitology, 45*: 261-283.

KERSHAW,W.E. (1955). The epidemiology of infections with *Loa loa. Transactions of the Royal Society of Tropical Medicine and Hygiene, 49*: 143 – 150

LANGELER, C., KILIMA, P., MSHINDA, H., MORONA, D., HATZ, C. TANNER, M. (1991). Rapid, low-cost, two-step method to screen for urinary Oschistosomiasis at the district level. The Kilosa Experience. *Bulletin of the World Health Organization, 69:* 179 – 189.

NWAORGU, O. C., OHAEGBULA, A., ONWELUZO, I. E., ALO, E. T., NWEKE, L. N., AGU, V. L. and EMEH, E. (1994). Result of a large scale onchocerciasis survey in Enugu State, Nigeria. *Journal of Helminthology, 68(2):* 155 – 159.

NOIREAU, F. APEMBET, J. D., NZOULANI, A. and CARME, B. (1990). Clinical manifestations of loiasis in an endemic area in the Congo. *Tropical Medicine and Parasitology, 41*: 37-39

OFOMATA, G. E. K. (1979). *Nigeria in Maps, Eastern States*. Ethiope Publishing House, Benin City, Nigeria.

OGUNBA, E. O. (1977). *Loa loa* microfilaraemia in the Nigerian population. *Tropical and Geographical Medicine, 29*: 51 – 55.

PINDER, M. (1988). *Loa loa*-a neglected filaria. *Parasitology Today, 4*: 279-284.

TWUM-DANSO, N. A. (2003). *Loa loa* encephalopathy temporally related to ivermectin administration reported from onchocerciasis mass treatment programs from 1989 to 2001: Implications for the future. *Filaria Journal 2 (suppl. 1),* 57

UDONSI, J. K. (1986 ). The status of human filariasis in relation to clinical signs in endemic areas of the Niger Delta. *Annals of Tropical Medicine and Parasitology, 80*: 425 -432

UFOMADU, G. O., NWOKE, B. E. B., AKOH, J. I. SATO, Y., EKEJINDU, G. O. C., UCHIDA, A., SIHWAKU, K., TUMBAU, M. and UGOMO, K. K. (1991 ). The occurrence of loiasis, mansonellosis and wuchereriasis in the Jawara River Valley, Central Nigeria. *Acta Tropica, 48*: 137 - 147 .

WHO/TDR (2001). Rapid assessment procedures for loiasis. Report of a multi-centre study. (Wanji, S. ed.) Document No TDR/IDE/RP/RAPL/01.1 Geneva, World Health Organization.