High prevalence of epilepsy in two rural villages in Mahenge area, Tanzania: after 20 years of community directed treatment with ivermectin.

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Background

- Epilepsy is a neurological disease characterized by unprovoked seizures.
- About 50 million people suffering from epilepsy.
- The prevalence is highest in low and middle income countries.
- In Tanzania, Uganda and South Sudan a distinctive form of epilepsy has been described as nodding syndrome (NS). And it has been reported occur in onchocerciasis endemic regions.
  - NS affects mainly children and besides the nodding seizures it causes mental retardation and debilitating physical development.

Background

- Although epidemiological studies underline the association of onchocerciasis and the onset of epilepsy, the causative mechanism is not yet understood.
- Onchocerciasis is a parasitic disease caused by the worm *Onchocerca volvulus* transmitted by blackflies.
- It is estimated that 37 million people worldwide are infested by *O. volvulus*, of whom 99% live in Africa.
- In infected persons, the adult female worms form subcutaneous nodules and release thousands of microfilariae daily leading to itching, dermatitis and if left untreated may results in blindness.
- Onchocerciasis is treatable through a long period of time with ivermectin, which kills the microfilariae and inhibits their release of microfilariae.
- WHO listed Onchocerciasis as a priority disease targeted for elimination by 2025.
- This study has been designed to test whether the implementation of CDTi decreases the incidence of epilepsy and NS in onchocerciasis endemic regions.

Study Objectives

Epilepsia, 33(6):1051–1056, 1992
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Prevalence and Incidence of Epilepsy in Ulanga, a Rural Tanzanian District: A Community-Based Study

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Summary: A random cluster sample survey of approximately 18,000 people in 11 villages was performed in Ulanga, a Tanzanian district with a population of approximately 139,000 people. Well-instructed fourth-year medical students and neurologic and psychiatry nurses identified persons with epilepsy using a screening questionnaire and sent them to a neurologist for detailed evaluation. Identified were 207 subjects (88 male, 119 female) with epilepsy; of these, 185 (89.4%) (80 male, 105 female) had active epilepsy. The prevalence of active epilepsy was 10.2 in 1,000. Prevalence among villages varied, ranging from 5.1 to 37.1 in 1,000 (age-adjusted 5.8–37.0). In a 10-year period (1979–1988) 122 subjects living in the 11 villages developed epilepsy, with an annual incidence of 73.3 in 100,000. Generalized tonic-clonic seizures (GTCS) accounted for 58% and partial seizures accounted for 31.9%, whereas in 10.1% seizures were unclassifiable. Of the partial seizures, secondarily generalized seizures were the most common. Possible etiologic or associated factors were identifiable in only 25.3% of cases. Febrile convulsions were associated in 13.4 of cases. Other associated factors included unspecified encephalitis (4.7%), cerebral malaria (1.9%), birth injury (1.4%), and other (3%). In 38% of the cases, there was a positive family history of epilepsy. **Key Words:** Epilepsy—Epidemiology—Prevalence—Incidence—Tanzania—Delivery of health care.

Methods

- The study was conducted in the Mahenge highlands in Ulanga district in Tanzania.
- Study site selection is based on an initial study on epilepsy in Mahenge area back in 1989 (Rwiza et al., 1989).
- Villages with highest prevalence in the past were included in the study.

Name of Village	Population size	Number of Epilepsy cases	Prevalence per 1000 people
Mdindo	539	20	37.1
Vigoi	1822	23	12.6
Misegesi	1667	18	10.8
Total	4028	74	18.37

Methods

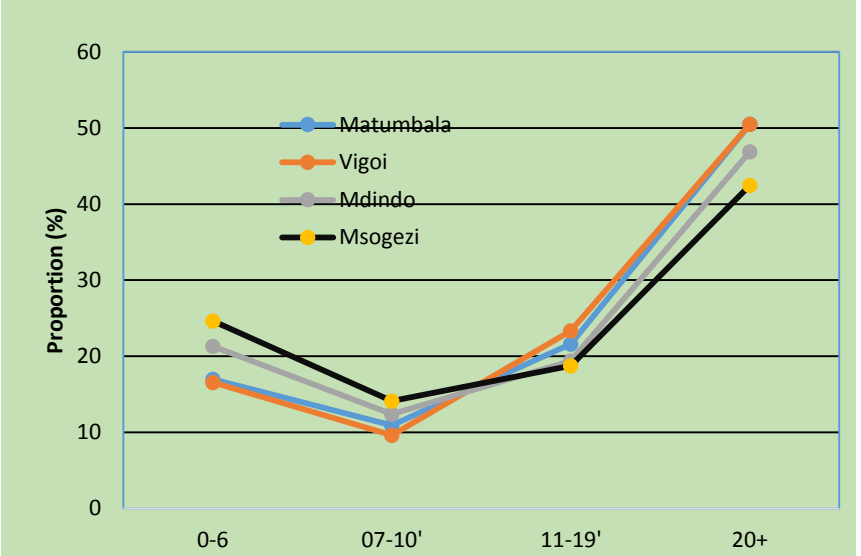
- Door-to-door households visits was implemented by village health workers to:
  - enumerate the village population and collect information on history of use of ivermectin
  - screened to identify individuals suspected to have epilepsy by using 5 validated questions
  - identify children for *onchocerca* serology as well as adults males for REMO
  - VHWs were taken through the households by community leaders for easy identification of households and introduction of study the team.
- Identified epilepsy suspects were referred to:
  - neurologist for further examination
- A sample of 50 adults (≥20 years) were also selected and referred clinicians for REMO assessments
  - All referred individuals were tested for onchocerciasis antibodies using OV16 rapid tests by lab technician.

Results

- A total of 1,168 households were visited and 5,117 individuals registered
- median age was 18.5 years (IQR 8.5 – 37.5); 53.2% were females.
- Msogezi had the youngest population (median age 15.4 years [IQR 7.1 – 31.5]) while Vigoi had the oldest population.
- 95% depended on farming as their primary economic activity.
- Predominant group was the Wapogoro (92.8%) out of 31 encountered.
- 244 (4.8%) individuals with suspected epilepsy were found and 239(97.9%) were examined by the neurologist

Table 1: Characteristics of the villages and population surveyed

Village	Mean altitude (range), mASL	No. of Households	No. of people	Median age (IQR)
Matumbala	1052 (786 – 1144)	244	972	20.1 (10.0 – 40.0)
Vigoi	1063 (504 – 1194)	388	1646	20.3 (10.5 – 40.4)
Mdindo	561 (444 – 802)	198	941	17.5 (8.5 – 38.1)
Msogezi	575 (491 – 731)	338	1558	15.4 (7.1 – 31.5)
Total		1168	5117	18.5 (8.7 – 37.5)

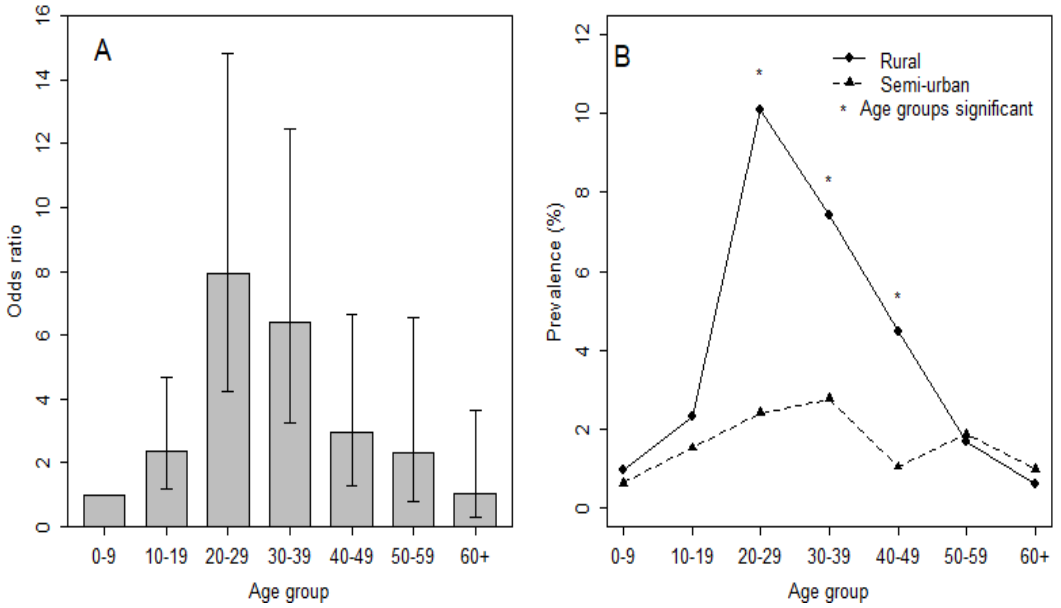


Population distribution by age group by village

Epilepsy screening and confirmed cases

- Overall prevalence of epilepsy was **2.48%**
- Epilepsy prevalence was higher in the rural villages of Mdindo (3.51%) and Msogezi (3.53%) than in the semi-urban villages of Matumbala (1.65%) and Vigoi (1.40%), p<0.001

- The risk of epilepsy increased with increasing age until the age group 20–29 years and declined thereafter
- The prevalence of epilepsy was significantly higher rural and the different by age groups between the two settings was significant at age group 20–29 to 40–49.
- Individuals aged 20–29 in the rural setting had the highest prevalence (10.1%), which declined progressively as age was increasing
- Multiple cases of epilepsy per household:
  - five households had two family members in Mdindo
  - one household had three and two households had two family members in Msogezi
  - All households with more than one person with epilepsy were of Wapogoro ethnicity with the exception of one household which was Wazigua.



Risk of epilepsy by age group when adjusted by study village (A) and prevalence of epilepsy by age group and strata (B)

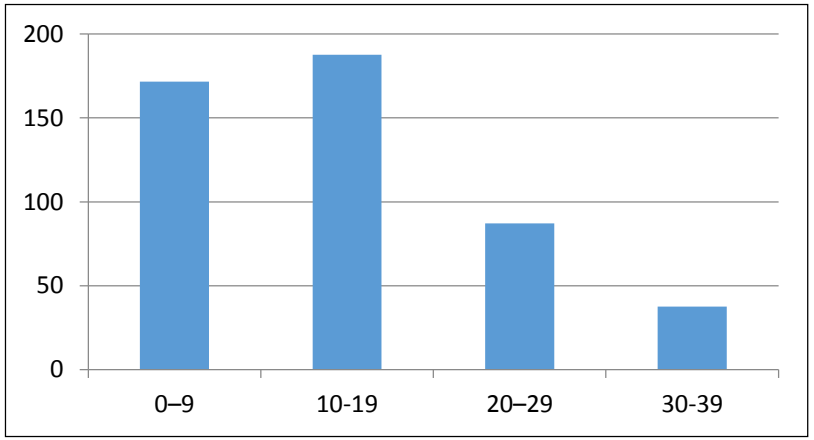
Incidence of epilepsy

- During the past 5 year period preceding the survey, 27 persons developed their first episode of seizures:
  - 111 (95%CI: 73 – 161) per 100 000 for all forms of epilepsy, (Table 5).
  - six of 19 individuals aged 3-18y had history of severe disease before the onset of the epilepsy (meningitis, malaria and comma, malaria and febrile seizure, malaria and meningitis, measles and last one had psychomotor retardation)
  - A total of 13 individuals aged 3-18 years had no specific severe condition before the onset of the epilepsy and were categorized as OAE events, giving an incidence rate of 131 (70–223)

Number of new cases of epilepsy over a 5 year period and incidence of epilepsy and OAE per 100,000 per year

	Overall Population				Population aged [3–18] years		
Village	Current population size (n)	# new cases	Incidence rate (95%CI)	Population size (n)	# new cases	# new OAE	Incidence rate (95%CI)
Matumbala	972	4	86.3	376	3	2	111.5
Vigoi	1,646	8	101.9	620	5	3	101.5
Mdindo	941	5	111.4	403	4	3	156.1
Msogezi	1,558	10	134.6	686	7	5	152.9
Total	5,117	27	111 (73–161)	2,085	19	13	131 (70–223)

Incidence by age group



Seizure types and frequency

Type of seizure	Freq.	%
Generalized tonic-clonic seizures	72	56.7
Atonic seizures (drop attacks)	22	17.3
Absences	9	7.1
Secondary generalised partial	8	6.3
Complex partial	3	2.4
Simple partial (focal) seizures (consciousness not lost)	2	1.6
Nodding syndrome (active)	13	10.2

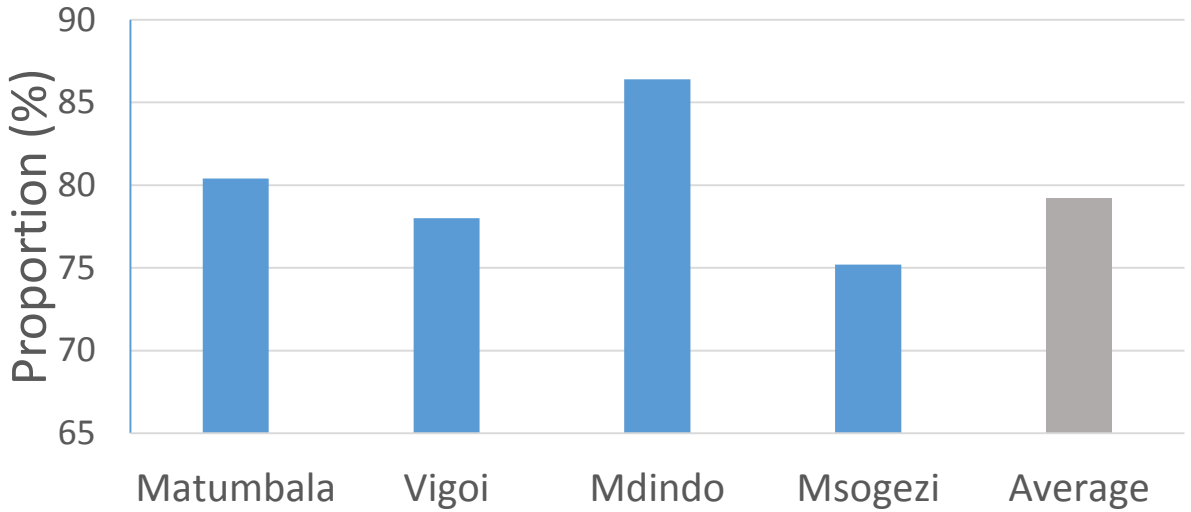
Seizure freq	Freq.	%
<1 per mon	61	57.55
<4 per mon	13	12.26
<7 per week	10	9.43
>7 per week	1	0.94
Others	21	19.81

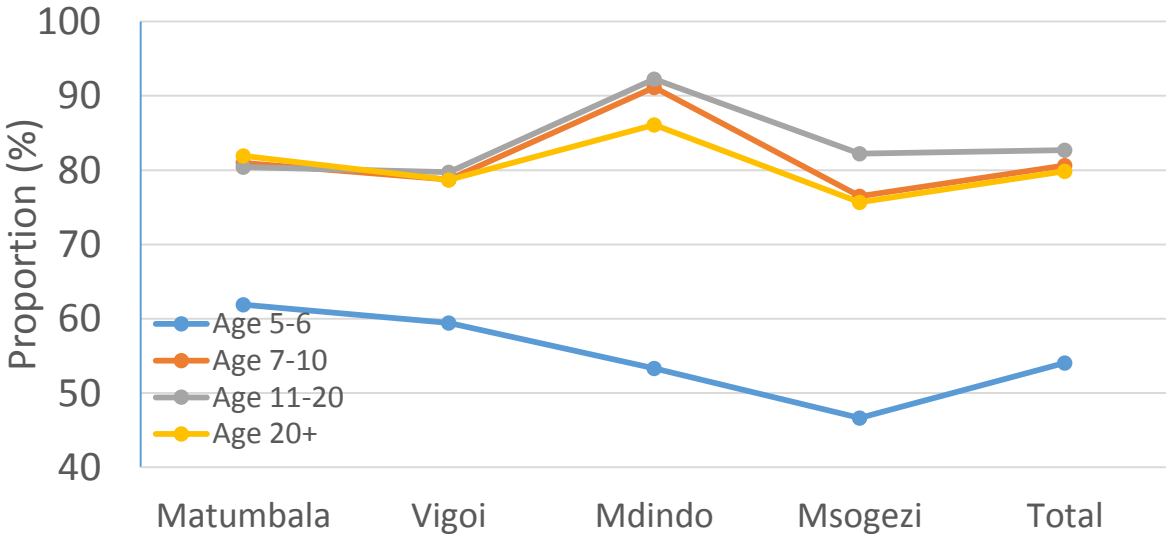
92% of NS came from a rural villages

- Generalized tonic-clonic was the frequently observed type of seizure
- Most of patients had less than one seizure per month

Ivermectin coverage in individuals aged ≥6 years

- High coverage (>80%) in Mdindo and Matumbala
- Low coverage in Msogezi (~75%)
- Low coverage in children 5-6 year with Msogezi leading downwards
- Individuals 11-19 years had slightly the highest coverage than the rest of other age groups





Rapid assessments of onchocerciasis transmission risk (6-10 yrs)

- 530 children aged 6–10 years were tested *O.volvulus* IgG4 antibodies using the OV16 rapid tests

- The prevalence of OV16 positive tests was 20.7%
  - The prevalence of positive OV16 tests was similar between the semi-urban villages (p = 0.98) and between the rural villages (p = 0.294)
  - but was lower in semi-urban (3.4%) than in the rural villages (38.4%) (p < 0.001).

- None of the children aged six years from the semi-urban villages were positive for the OV16 tests

- In the rural villages; children aged 6 years had the lowest prevalence (26.5%) and those aged 9 years had the highest (48.1%)

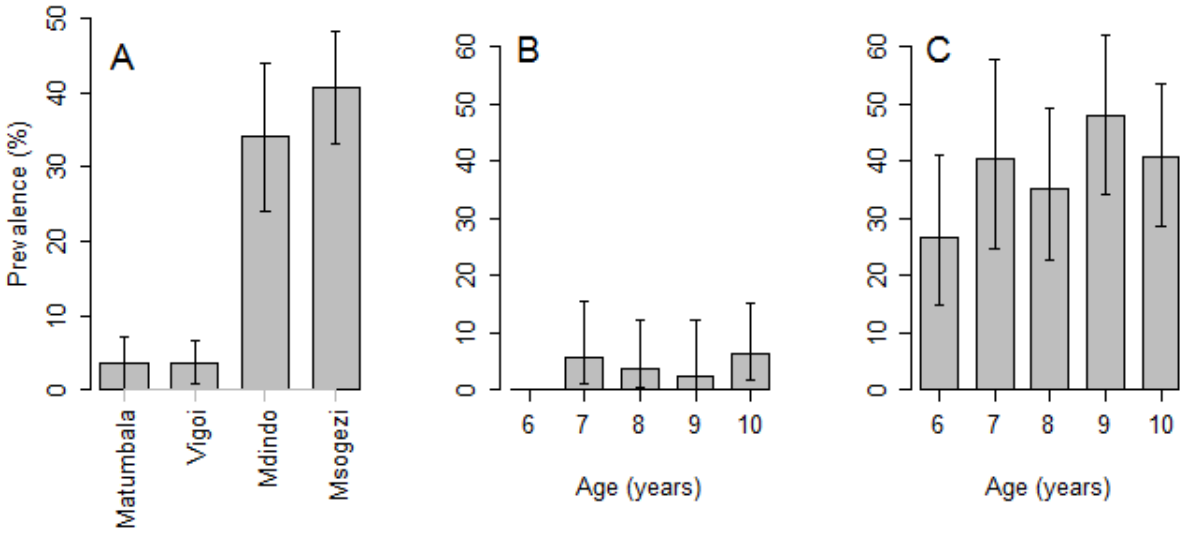


Figure 2: OV16 tests results in children aged 6-10 years by village (A), and by age as integer for urban (B) and rural villages (C)

Rapid epidemiological mapping of onchocerciasis

- 215 males (median age 40.2 years) were examined for presence of onchocerciasis nodules
- Only five (2.3%), one from Matumbala, one from Vigoi, and three from Mdindo village, were found to have nodules.
- Only one individual from Matumbala had two nodules, while the rest had one nodule only.
- Prevalence of positive OV16 rapid test in this group was high with rate been higher in the rural (76.5%) than in the semi-urban (50.6) villages, p<0.001.

Nodules and OV16 test results among adult males (≥ 20 years)

Village/Strata	N	No. with nodules (%)	Number screened (%)	% OV16 test +ve (95%CI)	χ^2-test (p-value)[δ]
Village					
Matumbala	35	1 (2.9)	34 (97.1)	32.3 (15.8 – 48.9)	
Vigoi	54	1 (1.9)	53 (98.1)	62.3 (48.8 – 75.8)	7.41 (0.006)
Mdindo	54	3 (5.6)	50 (92.6)	80.0 (68.5 – 91.5)	19.26 (<0.001)
Msogezi	72	0 (0)	69 (95.8)	73.9 (63.3 – 84.5)	16.42 (<0.001)
Strata					
Semi-urban	126	2 (1.6)	119 (94.4)	50.6 (39.9–61.3)	
Rural	89	3 (3.4)	87 (97.6)	76.5 (68.7–84.2)	14.9 (<0.001)
Total/Average	215	5(2.3)	206 (95.8)	65.5 (59.0 – 72.1)	

Association between onchocerciasis and epilepsy

- Prevalence of OV16 positive tests was higher in epilepsy patients (57.9% vs. 41.25%), UOR: 1.96 (1.09 – 3.53), p=0.025
  - Adjusting for age and village, the odds ratio changed to 1.81 (0.93 – 3.49), p=0.078.
  - The association between OV16 and epilepsy was more evident in individuals aged below 20 years (χ^2= 2.87, P = 0.090)

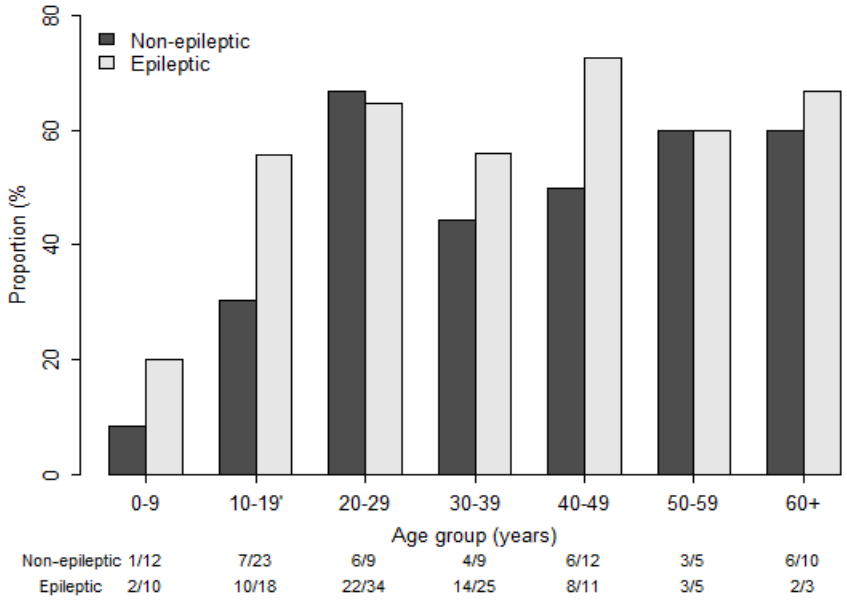
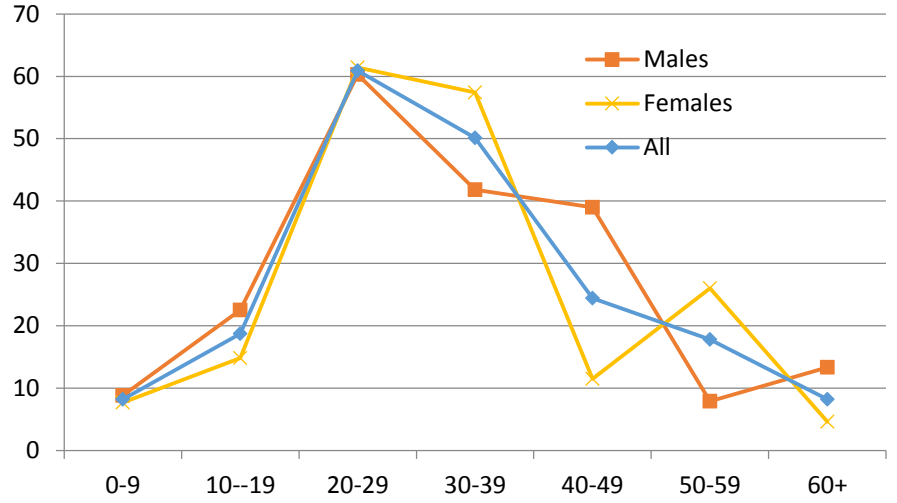


Figure 3: Distribution of OV16 positivity

Prevalence of Epilepsy by age group and gender per 1000 Popln.)

- High prevalence in 20-39 years
- Low prevalence in children <10 years
- Low prevalence in 60+ maybe due to early mortality
- High variability in cases between age 40-59 and between males and female.
  - May be due under or over stating of age of epilepsy patients
- Similar pattern of distribution of cases as in Rwiza et al.,
  - However, with low prevalence in 10-19yrs, suggesting less incidence of OAE in recent years.



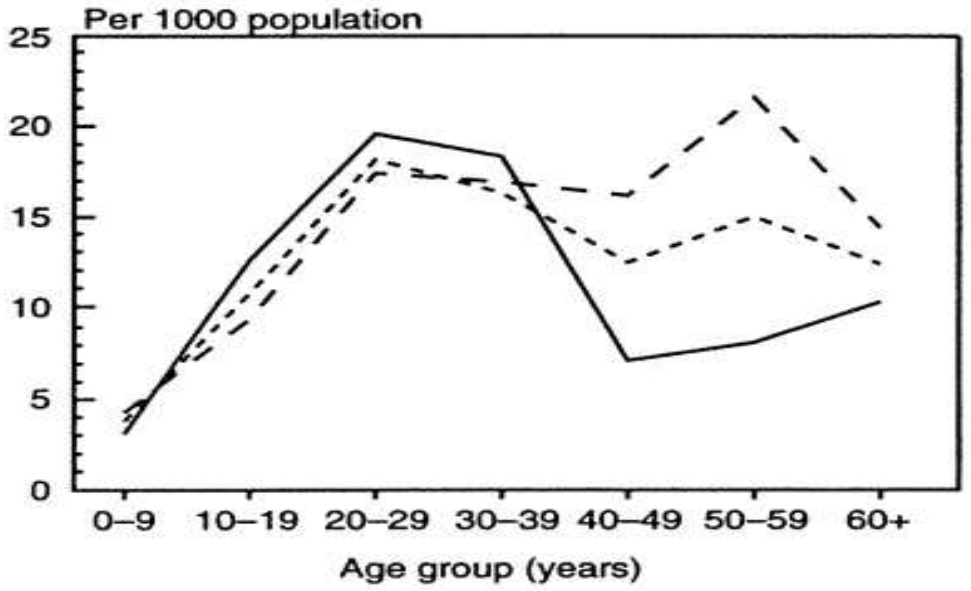


FIG. 1. Prevalence of active epilepsy (per 1,000 population) by age and sex, in Ulanga, Tanzania: Total (small-dotted line), women (large-dotted line), men (solid line).

Treatment of epilepsy

Drug/drug combination	Freq	%
Barbiturates	39	36.79
Barbiturates + Diphenylhydantoin	9	8.49
Barbiturates + Carbamazepin	1	0.94
Diphenylhydantoin	10	9.43
Carbamazepin	4	3.77
Carbamazepin + Herbal	1	0.94
Herbal	1	0.94
Not/Don’t know	41	38.68

Discussion

- This study has shown that still high prevalence of epilepsy is found in the four study villages, with prevalence rates been comparable to the 1989 survey
- High prevalence of epilepsy in rural settings
- Similar pattern of epilepsy prevalence by age as that shown in1989 survey which was mainly comprised of low risk population
- High prevalence of positive serology against onchocerciasis in children and adult individuals despite the long term (~20 years) of use of Ivermectin
    - High prevalence in adults may indicate low adherence to drug. According to clinician from Msogezi Dispensary, a good number of individuals from the village did not take Ivermectin last round due to it conceding with the season where most or people were away for faming activities. He was also on the opinion that majority declined to use the drug due perceived side effects (especially swelling)
    - Resistance against drug
    - High prevalence in young individuals indicate active transmission in the study areas.

Future developments

- To implement a multi-disciplinary approach to control onchocerciasis-associated epilepsy in the Mahenge area in Tanzania by:
  - Enhancing the multi-disciplinary research capacity concerning oncho and epilepsy/NS in Tanzania.
    - To establish an OAE research group in Tanzania which will be supported by experts from the UA and international experts linked to the NSETHIO project
    - Train one PhD student and one master students

- Implement research activities aimed towards reduction of rates oncho and epilepsy/NS in the Mahenge area.
  - establish a surveillance system for early detection and management of epilepsy/NS
  - Implement bi-annual treatment with the CDTi programme to better control oncho transmission and to decrease the incidence of OAE
  - Implement evidence-based guidelines to prevent and treat OAE by training local health care workers how to effectively diagnose and treat epilepsy/NS
  - Implement a community-awareness program to combat epilepsy/NS-associated stigma and discrimination.

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