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Relationships between Onchocerca volvulus microfilaraemia and the clinical manifestations of meso-endemic onchocerciasis in the Umuowaibu and Ndiorji communities in southeastern Nigeria

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Abstract

The study was aimed at determining the relationship between Onchocerca volvulus microfilaraemia and the clinical manifestations of onchocerciasis in the endemic Umuowaibu and Ndiorji communities in southeastern Nigeria. Two skin snips (each from the shoulder and the waist) were taken for parasitological examination from each individual during daytime using a Walser corneoscleral punch. These individuals were also examined for gradations of skin manifestations and visual impairments using standard criteria. In all, 62 (49.6%) of those with chronic skin damage were positive for O. volvulus microfilaraemia, whereas 317 (35.3%) of those without chronic skin damage were positive for O. volvulus microfilaraemia. This difference was significant ($\chi 2$-test; $p < 0.001$). The mf GMI of those with chronic skin damage (13 mf/snip) was significantly lower than the mf GMI of those without chronic skin damage (16 mf/snip) (t-test; $p < 0.001$). The mf prevalence of those with leopard skin (67.7%) was significantly higher than that in those without leopard skin (28.3%) ($\chi 2$-test; $p < 0.001$). The mf GMI of those with leopard skin was significantly higher than that of those without leopard skin (t-test; $p < 0.001$). Most cases of leopard skin were seen in those aged 20 years and above. Of those with subcutaneous nodules, 63.7% were O. volvulus mf positive, with an overall mf GMI of 19 mf skin snip. Among those without subcutaneous nodules, 28.0% were O. volvulus mf positive with an mf GMI of 14 mf/skin snip. These differences were statistically significant ($\chi 2$-test; $p < 0.001$; and t-test; $p < 0.001$). The prevalence of O. volvulus microfilaraemia was high among those who presented visual acuity problems with mf prevalence of 57.1% and mf GMI of 20 mf/skin snip. For those who did not present visual acuity problems, 35.5% were positive for O. volvulus microfilaraemia with mf GMI of 15 mf/skin snip. The difference in mf GMI was also statistically significant (t-test; $p < 0.001$). The difference in mf GMI was also statistically significant (t-test; $p < 0.001$). In conclusion, the O volvulus microfilaraemia was closely associated with most clinical manifestations especially among older age groups in the meso-endemic area.

Keywords: Onchocerciasis, chronic inflammatory skin damage, leopard skin, subcutaneous nodules, visual acuity, Onchocerca volvulus, Nigeria

1. Introduction

In Onchocerciasis is a debilitating parasitic infection of global public health importance, reported in 34 countries of the world (WHO, 1990), 26 of which are in Africa (WHO, 1987). About 90 million people are at risk infection, out of which 17.6 million are infected, including 326,000 people who have gone blind. About 7-10 million Nigerians are infected with Onchocerca volvulus, and approximately 40 million are at risk of the disease (WHO, 1996) with many thousands suffering from disabling complications of the disease (Anosike and Onwuliri, 1995; Uttah, 2009, 2010). One of the most significant onchocerciasis endemic areas in Nigeria is the hilly and undulating Udi-Enugu-Okigwe axis in the southeastern region, from where some rivers or their tributaries, supporting black fly vector breeding, have their origin (Uttah, 2010).

The Umuowaibu and Ndiorji communities are located in the Udi-Enugu-Okigwe axis, and are meso-endemic for onchocerciasis. The earlier parts of this study have been reported (Uttah, 2009, 2010). The overall prevalence was 37.0% and as high as 70.4% in the oldest age group (Uttah, 2010). The prevalence of the clinical manifestations related to onchocerciasis in the area included permanent itching (2.5%), onchodermatitis (3.9%), atrophy of the skin (5.8%), leopard skin (22.1%), and sowda (0.1%), subcutaneous nodules (25.3%), visual acuity problems (6.8%) (Uttah (2009). The clinical manifestations of onchocerciasis are intense in the area probably because of presence of endemic infections of other filarial species. This part of the study is aimed at determining the relationship between Onchocerca volvulus microfilaraemia and the clinical manifestations of onchocerciasis in the endemic Umuowaibu and Ndiorji communities in southeastern Nigeria.

2. Materials and methods

2.1 Study area and study population

The study was conducted in 2005 in two neighboring high altitude communities of Umuowaibu 1 and Ndiorji, in

Okigwe Local Government area of Imo State, Nigeria. The two communities with a combined population of 1,116 at the time of this study are socio-culturally similar, both inhabited by Ndiigbo, the majority tribe in southern, Nigeria. A familial settlement pattern was evident in the area with houses arranged in family clusters. A total of 381 houses were recorded in the two communities. Further details about the study area are given in Uttah (2010).

2.2 Skin snipping

Two skin snips (one from the shoulder and one from the waist) were taken for parasitological examination from each individual during daytime using a Walser corneoscleral punch. The details of the laboratory procedures for processing of, and the microscopical examination of the biopsies have been reported in Uttah (2010). The biopsies were placed in micro-titer wells containing 0.2 ml of 0.85% saline solution. When completed, each plate was covered with cellophane tape and taken to the laboratory where it was kept for 24 hours at room temperature. At the end of the 24-hour incubation period, the skin biopsies were fixed in formalin solution (35% formaldehyde solution) by adding two drops per micro-well. Thereafter, emerged microfilariae were observed and counted microscopically using x 40 magnification.

2.3 Clinical surveys

Informed oral consent was obtained from all adults and from parents or guardians of children aged ≤ 15 years, before any examination was carried out. Those who were sick with minor ailments were given medicine. Individuals were examined for various gradations of skin manifestations and visual impairments by qualified medical doctors using the criterion shown below:

Skin manifestations were graded as follows: Normal (0); Permanent itching without onchodermatitis (1); Onchodermatitis (with papules/thickening of skin/secondary infections (2); Atrophy of skin, loss of elasticity, paper thin skin (prematurely aged) (3); Mottled depigmentation (leopard skin) (4); Sowda (hyperpigmented thickened skin, unilateral)(5); and Hanging groin (6).

Visual impairments were graded as follows: No visual impairment (read as 6/18 or better in Snellen Chart)(0); Visual impairment (3/60 < reads< 6/18 in Snellen Chart)(1); Severe visual impairment (3/60 < reads < 6/60 in Snellen Chart)(2); Blind (inability to read (3/60 in Snellen Chart)(3).

2.4 Data analysis

The Epi-Info version 6 .0 was used in entering data from parasitological survey, and SPSS for windows (1995 version) was used for data analysis. The geometric mean intensity (GMI) of microfilariae was calculated as antilog (Σlog (x+1)/n), with x being the number of mf per ml of blood in microfilaraemic individuals and n the number of microfilaraemic individuals examined.

3. Results

The relationships between O. volvulus microfilaraemia and the four clinical manifestations of onchocerciasis in the study area namely, chronic inflammatory skin damage, leopard skin, subcutaneous nodules, and visual acuity problems, were analyzed.

3.1 The relationship with chronic inflammatory skin damage

The relationship between O. volvulus microfilaraemia and chronic inflammatory skin damage is presented in Table 1. A total of 62 (49.6%) of those with chronic skin damage were positive for O. volvulus microfilaraemia, whereas 317 (35.3%) of those without chronic skin damage were positive for O. volvulus microfilaraemia. This difference was statistically significant (χ2-test; $p < 0.001$). The mf GMI of those without chronic skin damage (16 mf/snip) was significantly higher than the mf GMI of those with chronic skin damage (13 mf/snip) (t-test; $p < 0.001$).

The majority of cases of chronic skin damage were seen in those ≥ 10 years old, and in this group the mf prevalence among those with chronic skin damage was significantly higher than the mf prevalence of those without chronic skin damage (χ2-test; $p < 0.001$), whereas the mf GMI of those without chronic skin damage was significantly higher than the mf GMI of those with chronic skin damage (t-test; $p < 0.001$).

3.2 Relationship with leopard skin

The relationship between O. volvulus microfilaraemia and leopard skin is presented in Table 2. The mf prevalence of those with leopard skin (67.7%) was significantly higher than that in those without leopard skin (28.3%) (χ2-test; $p < 0.001$). The mf GMI of those with leopard skin was significantly higher than that of those without leopard skin (t-test; $p < 0.001$). Most cases of leopard skin were seen in those aged 20 years and above. Among these, the mf prevalence of those with leopard skin was significantly higher than the mf prevalence of those without leopard skin (χ2-test; $p < 0.001$), and the mf GMI of those with leopard skin was also significantly higher than that of those without leopard skin (t-test; $p < 0.001$).

3.3 Relationship with occurrence of subcutaneous nodules

Relationship between O. volvulus microfilaraemia and occurrence of subcutaneous nodules is presented in Table 3. Of those with subcutaneous nodules, 63.7% were O. volvulus mf positive, with an overall mf GMI of 19 mf skin snip. Among those without subcutaneous nodules, 28.0% were O. volvulus mf positive with an mf GMI of

14 mf/skin snip. These differences were statistically significant (χ2-test; $p < 0.001$; and t-test; $p < 0.001$). All the cases of subcutaneous nodules were seen in those aged 10 years and above. Among these, the mf prevalence in those with subcutaneous nodules was significantly higher than in those without subcutaneous nodules (χ2-test; $p < 0.001$), and the difference in mf GMI between those with and those without subcutaneous nodules was statistically significant (t-test; $p < 0.001$).

3.4 The relationship with visual acuity

The relationship between O. volvulus microfilaraemia and visual acuity is presented in Table 4. The prevalence of O. volvulus microfilaraemia was high among those who presented visual acuity problems with mf prevalence of 57.1% and mf GMI of 20 mf/skin snip. For those who did not present visual acuity problems, 35.5% were positive for O. volvulus microfilaraemia with mf GMI of 15 mf/skin snip. The difference in mf GMI was also statistically significant (t-test; $p < 0.001$). The difference in mf GMI was also statistically significant (t-test; $p < 0.001$). Among those ≥ 20 years old, the difference in mf prevalence between those with and those without visual acuity problems was not statistically significant (χ2-test; $p > 0.05$), but the difference in mf GMI was statistically significant (t-test; $p < 0.001$).

4. Discussions

Onchocerca volvulus microfilaraemia was common among those who had chronic inflammatory skin damage. The prevalence and intensity of O. volvulus microfilaraemia was higher among those with leopard skin than among those without. This is in line with earlier studies in Nigeria (Edungbola et al., 1983, 1987; Akogun et al., 1992a), and confirms the high predictive relationship between leopard skin and O. volvulus microfilaraemia (Akogun, 1992). Furthermore, the leopard skin prevalence has been related to onchocercal Endemicity in several studies (Fuglsang, 1983; Edungbola et al., 1983, 1986, 1987). Like other symptoms, leopard skin is dependent on the intensity of microfilaraemia. Leopard skin may be linked to repeated scratching following blackfly bites (McMahon and Simonsen, 1995). The mean microfilarial density correlates well with the prevalence of leopard skin and that of lymphatic enlargement (Akogun et al., 1992b). Leopard skin observations as a tool for rapid community assessment would have a low sensitivity but a high specificity (Abanobi et al., 1994). The reason for this low sensivity is that leopard skin is a late stage manifestation of onchocerciasis.

The prevalence of leopard skin reported here exceeds that reported from the Jos area in the savannah zone (Nwoke, 1986). Leopard skin is probably more prevalent in the forest zone than in the savannah zone (Abanobi et al., 1994). It is note worthy that ignorance of the etiology of leopard skin is widespread in the study population. Some believe it is due to the dew-soaked forests they pass through early mornings on their way to their farms, others attribute it to nwammi, the local name of blackflies and one woman attributed it to a medicated bathing soap she began using some months previously.

The prevalence and intensity of Onchocerca volvulus microfilaraemia was high among those presenting subcutaneous nodules. This is consistent with findings by Akogun et al, (1992a) who also noted that the nodule prevalence can be used to estimate the prevalence of O. volvulus in an endemic community. This is logical since subcutaneous nodules are known to be subcutaneous granulomas resulting from tissue reactions around adult worms (McMahon and Simonsen, 1995).

Most nodules were sited in the lower region of the body. In contrast, Akogun et al. (1992a) observed a majority of nodules in the iliac and ribeage in the savannah area of the Taraba River Basin. In the present study, nodules were not found in the ribeage. Geographical differences in location of nodules are well known. The location of nodules appear to reflect sites of inoculation of microfilariae (Akogun et al., 1992a), and different vector species and even strains may bite at different parts of the body. For example, while Simulium ochreacum bites primarily at the upper half of the body, S. damnosum bites more in the lower half. However, the involvement also of genetic factors may not be ruled out. The high concentration of subcutaneous nodules of savannah O. volvulus in the upper part of the body links well with the ocular involvement in savannah onchocerciasis. Similarly, the relatively high concentration of subcutaneous nodules in the lower half of the body in rainforest onchocerciasis links with limited ocular involvement here. Furthermore on nodules, the belief that microfilariae are most common in the vicinity of the nodules is not universal. Kershaw et al. (1954) noted that in early infections, where there were only few nodules. The few microfilariae present were found close to nodules, whereas in cases of more advanced infections. The distribution of microfilariae is largely independent of the exact position of the nodules. In addition, the concentration is highest in lichenified skin (Kale, 1982).

Onchocerciasis in the Upper Imo River Basin is the forest type, and therefore, little or no onchocercal ocular involvements are expected (Budden, 1963; Duke et al., 1966). A high prevalence of microfilaraemia was observed among those presenting than those not presenting visual acuity problems, especially among the older individuals. The involvement of O. volvulus microfilaraemia in visual impairments in the Imo Rover Basin is doubtful, since occupational practices such as fish smoking might be responsible for them (Uttah et al., 2004).

The association between filariasis clinical manifestations and microfilaraemia is not fully understood, but some previous studies in other filarial species have reported that microfilaraemia was common among those with clinical manifestations. For example, microfilaraemia was common among males who had hydrocele (Estambale et al., 1994; Taylor, 2002). Similarly microfilaraemia was common among individuals who had limb elephantiasis, and also among those with scrotal elephantiasis (Uttah, 2011).

The causal relationship between filarial infection and disease has been explained to result from death of microfilariae (Michael et al., 1994), from microbial involvement (Pani et al., 1995), or due to maternal infection status (Ravinchandran et al., 1997). Perhaps, the diversity of clinical responses to filarial infection is due to the intensity and type of immune response to the parasite or parasite products (king and Nutman, 1991); the ongoing intense exposure to infective parasite stages which modifies the immunologic profile and its associated pathology (King et al, 2001). This suggests that decreasing transmission intensity will disproportionately decrease pathology. Since the parasite does not replicate within the human host, the cumulative and/or temporal pattern of exposure to infective larvae determines the infection load and may therefore increase the likelihood of developing disease (Michael et al., 2001).

Overall, the causal relationship between onchocerciasis clinical manifestations and microfilaraemia may be a product of many interacting factors and may therefore present different pictures in different endemic areas and regions. Onchocerciasis is meso-endemic in Umuowaibu and Ndiorji communities of south-eastern Nigeria. The high prevalence of microfilaraemia and the chronic clinical manifestations observed there underscore the need for renewed awareness campaign to bring the attention of individuals in endemic areas to the importance of personal protective measures against the infective bites of the blackfly vector. This is also a wake-up call to health authorities to urgently combat this debilitating scourge by implementing the combination therapy interventions.

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Table 1. Relationship between *O. volvulus* microfilaraemia and chronic inflammatory skin damage

Age group (years)	Individuals with chronic inflammatory skin damage			Individuals without chronic skin damage		
	No.	No. mf positive (% prevalence)	GMI (mf/snip)*	No.	No. mf positive (% prevalence)	GMI (mf/snip)*
1-9	4	2 (50.0)	-	205	27 (13.2)	12
10+	121	60 (49.6)	13	694	290 (41.8)	17
Total	125	62 (49.6)	13	899	317 (35.3)	16

*Only indicated if there are ≥ 3 mf positive cases

Table 2 Relationship between *O. volvulus* microfilaraemia and leopard skin

Age group (years)	Individuals with leopard skin			Individuals without leopard skin		
	No.	No. mf positive (% prevalence)	GMI (mf/snip)*	No.	No. mf positive (% prevalence)	GMI (mf/snip)*
1-19	2	0 (0.0)	-	466	88 (18.9)	13
20+	224	153 (68.3)	19	332	138 (41.6)	14
Total	226	153 (67.7)	19	798	226 (28.3)	14

*Only indicated if there are ≥ 3 mf positive cases

Table 3 Relationship between *O. volvulus* microfilaraemia and occurrence of subcutaneous nodules

Age group (years)	Individuals with subcutaneous nodules			Individuals without subcutaneous nodules		
	No.	No. mf positive (% prevalence)	GMI (mf/snip)*	No.	No. mf positive (% prevalence)	GMI (mf/snip)*
1-19	0	0 (0.0)	-	209	29 (13.9)	11
20+	259	165 (63.7)	19	556	185 (33.3)	14
Total	259	165 (63.7)	19	765	214 (28.0)	14

*Only indicated if there are ≥ 3 mf positive cases

Table 4 Relationship between *O. volvulus* microfilaraemia and visual acuity problems

Age group (years)	Individuals with visual acuity problems			Individuals without visual acuity problems		
	No.	No. mf positive (% prevalence)	GMI (mf/snip)*	No.	No. mf positive (% prevalence)	GMI (mf/snip)*
1-19	1	0 (0.0)	-	467	88 (18.8)	13
20+	69	40 (58.0)	20	487	251 (51.5)	16
Total	70	40 (57.1)	20	954	339 (35.5)	15

*Only indicated if there are ≥ 3 mf positive cases