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Concurrence of dermatological and ophthalmological morbidity in onchocerciasis

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ABSTRACT

Prevalence of skin and eye disorders in African onchocerciasis (river blindness) is well documented. However, less is known about their joint occurrence. Information on concurrence may improve our understanding of disease pathogenesis and is required to estimate the disease burden of onchocerciasis. We analysed data from 765 individuals from forest villages in the Kumba and Ngamba Health districts, Cameroon. These data were collected in 1998, as baseline data for the evaluation of the African Programme for Onchocerciasis Control. Concurrence of symptoms was assessed using logistic regression. Onchocerciasis was highly endemic in the study population (63% nodule prevalence among males aged ≥ 20). Considerable overall prevalences of onchocercal visual impairment (low vision or blindness: 4%), troublesome itch (15%), reactive skin disease (19%), and skin depigmentation (25%) were observed. The association between onchocercal visual impairment and skin depigmentation (OR 9.0, 95% CI 3.9–20.8) was partly explained by age and exposure to infection (OR 3.0, 95% CI 1.2–7.7). The association between troublesome itch and reactive skin disease was hardly affected by adjustment (adjusted OR 6.9, 95% CI 4.2–11.1). Concluding, there is significant concurrence of morbidities within onchocerciasis. Our results suggest a possible role of host characteristics in the pathogenesis of depigmentation and visual impairment. Further, we propose a method to deal with concurrence when estimating the burden of disease.

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1. Introduction

Onchocerciasis or river blindness is caused by the nematode *Onchocerca volvulus*. Infective larvae are transmitted

between human hosts by the blackfly vector *Simulium* which breeds in river rapids. Adult female worms produce millions of larvae or microfilariae during their 10 year lifespan.¹ These microfilariae migrate through the human body and cause deforming skin disease, severe itch and visual loss.² Onchocerciasis is endemic in large parts of sub-Saharan Africa. In Cameroon alone, at least 6.4 million people live in endemic areas that are currently subject to mass treatment with ivermectin.³ Although there is

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ample information about the prevalence of onchocercal morbidity, we are aware of only one paper that explicitly describes concurrence of skin and eye disease in individuals. Browne reported that 42% of subjects with onchocercal ocular lesions also suffered from skin depigmentation compared to only 4% of all infected individuals.⁴ It was not described whether similar overlap occurs between other ocular and skin manifestations; also, the biological mechanisms behind this concurrence were not clear.

In depth analysis of data on concurrence may enhance our understanding of the pathogenesis of onchocerciasis. To date, it has been established that vision loss and blindness are most likely the result of progressive, cumulative tissue damage caused by microfilariae, as indicated by the increasing prevalence and incidence of ocular morbidity with age in stable endemic areas.^{5–9} Further, onchocercal skin disease is thought to be partly mediated by genetic predisposition. For instance, a number of onchocercal skin manifestations have been linked to specific host immune responses^{10,11} and polymorphisms in genes encoding important parts of the human immune system.^{12–16} However, the relative importance of cumulative exposure to infection and genetic predisposition in the development of morbidity is still unclear. Analysis of patterns in concurrence of morbidity may clarify this. For example, clustering of symptoms may occur in individuals with the longest experience of infection, or heaviest infection load. Alternatively, history of infection and infection load may not explain concurrence very well, suggesting that genetic or behavioural factors play a role.

Information about concurrence of clinical manifestations is required for calculating the burden of disease in terms of disability-adjusted life years (DALYs) lost per year. Disability-adjusted life year calculations preferably include all forms of morbidity that cause a significant loss of health at population level, either due to high severity or high prevalence. In the case of onchocerciasis, this means that symptoms of both skin and eye disease should be included. Of course, more than one type of symptom can be present in an individual. This is important because the loss of quality of life or life years due to a specific symptom may be influenced by the presence of another symptom. Therefore, simply calculating and summing the burden of disease for each separate symptom may lead to biased estimates of the overall burden of onchocerciasis-related morbidity in a population.¹⁷ For example, because individuals with onchocercal skin depigmentation are already stigmatised, the loss of quality of life from reactive skin disease due to onchocerciasis may be different than in otherwise healthy individuals. Knowledge about patterns in concurrence allows us to decide how to deal with such overlaps (also see section 3).

In this study, data from a cross-sectional population survey in two forest areas of Cameroon were used to explore patterns in concurrence of four main types of onchocercal morbidity: skin depigmentation, reactive skin disease (RSD), severe itch and onchocercal visual impairment. Concurrence was quantified by means of logistic regression analysis, while adjusting for proxies for cumulative exposure to infection, in particular age and

indicators of infection (presence of nodules and presence of microfilariae in the anterior chamber of the eye).

2. Materials and methods

2.1. Study sites

We performed a secondary analysis on data that were collected in 1998 as baseline data for the impact assessment study of the African Programme for Onchocerciasis Control (APOC). APOC performed surveys in ten sites, which all met predefined selection criteria: they were mesoendemic or hyperendemic for onchocerciasis as determined by earlier rapid epidemiological mapping of onchocerciasis (REMO) studies (>20% nodule prevalence in males \geq 20 years old)¹⁸ and less than 25% of the general population had received clinic-based treatment during the previous five years. For the current analysis we used data from two of the 10 sites, which were considered sufficient for the purpose of the study. We used the data from two sites in Cameroon, which was a pragmatic selection, because these data were best documented and could be processed most easily.

The first study site was situated in the Health district of Ngambe in the Littoral Region. This district has about 100 000 inhabitants and is characterised by forest and the traversing River Sanaga. The study examinations were performed in July and August 1998, during the short dry season. The second study site was situated in the southwest province of Cameroon, in the Kumba Health District (approximately 100 000 inhabitants). This district is characterised by tropical forest and has both a dry and a rainy season. Here, the examinations took place in November and December 1998 during the dry season. At both sites, *Simulium squamosum* is the only vector for transmission of onchocerciasis. A more detailed description of the study areas can be found elsewhere.¹⁹

2.2. Data collection

Prior to the surveys, a list of villages in each site was compiled. Next, a team of social scientists carried out a census of the population in the communities, starting in a given village, and progressing to the neighbouring ones until at least 1500 persons were recorded in each site. Individuals aged five years and older were asked to present themselves for examination at a central point in the village. In light of future evaluations of the APOC, a minimum sample of 750 subjects per site was taken to be able to detect an absolute 10% reduction in prevalence of onchocercal skin disease over time. Because ophthalmological examinations take longer than dermatological examinations and require more cooperation from the subject, only half of the individuals were examined ophthalmologically (every other individual of 10 years or above).

Subjects who underwent examination were asked about their educational level. It was recorded whether subjects followed – but not necessarily finished – secondary or primary education, or had followed none at all. Furthermore, each individual was questioned about symptoms typical of onchocerciasis. Severe itch was defined as 'itch associated with insomnia. Responses were marked as 'spontaneous'

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