Systematic Review on Onchocerciasis Infection in Nigeria in the Past Five Decades

Ezeh Charles Ogbonna, Odama Richard Ikani*

ABSTRACT

Onchocerciasis is a serious neglected tropical disease caused by the filarial nematode *Onchocerca volvulus*, transmitted by black fly which leads to blindness and chronic disability with estimated infection rate of about 37 million people in tropical Africa and in isolated foci in Yemen and Latin America and has caused a debilitating eye and skin disease in more than 5 million people with about 1.2 million visual impairment or blindness and half of this population residing in Nigeria. **Background:** Onchocerciasis or river blindness results from infestation by the nematode *Onchocerca volvulus*, characterized by eye affections and skin lesions with severe troublesome itching. It is a chronic, communicable, slowly progressive, parasitic disease which has being rated as the second-leading infectious cause of blindness worldwide annually. It is a neglected tropical disease of great public health concern which is transmitted by black fly with estimated infection rate of about 37 million people in tropical Africa and in isolated foci in Yemen and Latin America. It has caused a debilitating eye and skin disease in more than 5 million people with about 1.2 million visual impairment or blindness and an estimate of over 85 million people leaving in endemic areas with 99% of the cases resulting from Africa and half of this population residing in Nigeria. Also, estimate of about 120 million people are at a risk of contracting the disease due to the breeding habit of the vector. **Methods:** The databases Medline, WHO website, CDC website, PubMed, Web of Science World Factbook of Central Intelligence Agency, were searched for relevant studies published for the past five decades on onchocerciasis in Nigeria. Papers investigating it prevalence, clinical features, diagnosis, treatment, government policy, world health organisation policy and recent findings as well as further finding in Nigeria were included. **Results:** Extrapolation of data from the past five decades on onchocerciasis infection in Nigeria has shown that the rate of infection is significantly reduced in certain areas of the country due to repeated administration of Ivermectin. However, in most regions the infection rate still persist with a percentage of up-to 24 (75%), 45.2%, lizard skin and leopard skin were seen in 3.5% and 2.0% respectively, hanging groin 2.6% and scrotal enlargement at 8.6%, (Bakundu district of Taraba state with infection rate in excess of 30%), 54.2% (Ibarapa Local Government Area of Oyo state), 61% and 71% (Kuhe and Gube community of Benue state), 83% (Ona North Local Government Area of Edo state) and certain patients were blind due to onchocerciasis and were positive to onchocerciasis test. 79.5% in Oyo state (159 patients tested positive for onchocerciasis out of 200 patients), 94.5% in Kaduna state, (189 patients tested positive for onchocerciasis out of 200 patients). **Conclusion:** The results of this systematic review suggest that there have been a significant decrease in onchocerciasis infection in several regions of the country. However, the prevalence still persists mostly in river line area and regions which are inaccessible to the program as well as lack of orientation on the disease. Also, government policy on how often is Ivermectin made available to the people and making provision to reach these areas yet covered and the decreased in larvae control have also contributed to the high prevalence of the disease in Nigeria. This accounts for the reason why over 40% of the world prevalence rate is from Nigeria. **Key words:** Onchocerciasis, Epidemiology, Nigeria, Ivermectin, Moxidectin.

INTRODUCTION

Onchocerciasis is a serious neglected tropical disease caused by the filarial nematode *Onchocerca volvulus*, transmitted by black fly which can lead to blindness and chronic disability.¹ The filaria are group of tissue dwelling nematodes of vertebrate that are spread by blood feeding arthropods, *Onchocerca volvulus.*²³ With estimated infection rate of about 37 million people in tropical Africa and in isolated foci in Yemen and Latin America,²³ causing a debilitating eye and skin disease in more than 5 million people and about 1.2 million visual impairment or blindness.³ It is estimated that over 85 million people are leaving in endemic areas with 99% of the cases resulting from Africa and half of this population residing in Nigeria.³⁻⁸ Also, estimate of about 120 million people are at a risk of contracting the disease due to the breeding habit of the vector.³ It is more severe along the major rivers in the northern and central of the continent with
severity declining in villages farther from the river. Onchocerciasis has been the second leading infectious cause of blindness in the world. Long-term onchocercomata may also cause scarring, degeneration, loss of skin elasticity and disfiguration. Hence, Onchocerciasis related blindness alone has been estimated to reduce life expectancy by 4-10 years, as well as having an effect on the host ability to assimilate into their society with other skin related diseases.

Since 1970's, the World Health Organisation (WHO), International foundation, Non-Governmental Organisation and Government Organisations have worked co-operatively to reduce the burden of Onchocerciasis, through the use of insecticide sprays as well as biannual administration of Ivermectin; which has had positive effect in the fight against the disease in several parts of the world. In Africa alone, an estimated 600,000 cases of blindness had been prevented by 2002 and as at 2007, over 69 million doses of Ivermectin were supplied through Mectizan Donation Program. However, in much central part of Africa, concomitant infection with loa loa has shown precipitate toxic encephalopathy in patients on treatment with Ivermectin, and irreversible severe neurological events and health effect. Therefore, there is limitation on the use of Ivermectin in much central part of Africa as well as reliance on a single drug also increasing the potential for the emergence of Ivermectin-resistant Onchocerca volvulus, making development of new drugs or novel therapies imperative and the need for annual review to extrapolate the progress of it elimination.

**Epidemiology of Onchocerciasis in Nigeria**

Nigeria is the most populous nation in Africa which lies between latitude 4°N and 14°N and longitude 2° and 15°E, characterised by location of the largest mangrove in Africa, largest river delta, tropical rainforest climate, forest zone in the southern portion, with approximately 200 million people. It is estimated that 17 million people are at risk of the disease while 7-10million people are infected. Consequently, Nigeria has been estimated to account for nearly 40% of the world's prevalence of onchocerciasis.

A survey carried out by Noma on 20 countries participating in African Programme for Onchocerciasis Control (APOC) showed that Nigeria fall among the high risk countries with about 26 million after the Democratic Republic of Congo. Also, a research carried out by Adesina in the village of Idoani in Ondo state, Nigeria showed that a total of 24 (75%) from his 32 subjects examined were positive for onchocerciasis infection, with a >30 years old woman totally blinded and several individual with lizard skin features as a result of onchocerciasis infection. More so, in the community of Kuhe and Gube of Benue state of Nigeria, a research on 546 persons showed a high prevalence of onchocerciasis at 61% and 71% respectively, as well as an epidemiological study carried out in fourteen communities of Bakundi districts of Taraba state which showed that out of 1366 adults males involved in the study, 45.2% were infected with ten communities having an infection rate in excess of 30%, lizard skin and leopard skin were seen in 3.5% and 2.0% respectively, hanging groin 2.6% and scrotal enlargement at 8.6%. Furthermore, Opera shows that certain patients were blind due to onchocerciasis and were positive to onchocerciasis test. However, it is believed that there was a significant decrease in onchocerciasis in lower cross river basin due to repeated administration of Ivermectin.

This is in accordance with the various data from different part of Nigeria by various researchers, with its rate of occurrences as reported by these researchers varying from one geographical area to another with highest endemicity of 83% recorded in Oria North Local Government Area of Edo state. 79.5% in Oyo state (159 patients test positive for onchocerciasis out of 200 patients), 94.5 % in Kaduna state, (189 patients tested positive for onchocerciasis out of 200 patients) and 54.2% in Ibarapa Local Government Area of Oyo state. These data and lots more shows that Nigeria fall among the high risk countries on the list of 20 African Programme for Onchocerciasis Control (APOC) countries with about 26 million after the Democratic Republic of Congo. (Figure 1) In view of the efforts by the World Health Organisation (WHO), International foundation, Non-Governmental Organisation and Government Organisations who have worked co-operatively toward the elimination of this disease through the establishment of the Africa Programme for Onchocerciasis Control (APOC) and it transition into the Expanded Special Project for the Elimination of Neglected Tropical Disease in Africa (ESPEN), with the main strategy been the establishment of sustainable community-directed treatment with Ivermectin (CDTI) and vector control with environmentally safe method where appropriate. An annual review is imperative to ensure the availability of updated data on areas which need more Ivermectin administration as this will aid in achieving the goal of world free onchocerciasis by 2025.

**Clinical Features of Onchocerciasis**

The microfilaria; onchocerca volvulus mature into larvae in the gut of black fly of the genus Simulium. These leaves to the proboscis of the black fly and are introduced to the human bloodstream when fly take blood meals. In humans, the larvae migrate to various parts of the body but most often the skin and eyes and form nodules referred to as onchoceroma, typically seen in the skin, around joints and other bony prominence.

Onchocerca volvulus larvae mature into their sexually competent adult forms in these nodules. Male worms may move between nodules to fertilize female worms. Fertilized female worms then produce microfilaria which are released into the blood stream and picked up when new Simulium black flies feed from infected humans. The production of microfilaria by female adult worms depend on their associated Wolbachia endosymbiont. Developed adult worms cluster in the subcutaneous nodules (onchocercomata) with generalized pruritus in early infection and if the infection becomes severe, symptoms may include; Skin rashes, Ex-treme itching, Change of the skin pigmentation, Loss of skin elasticity which can make skin appear thin and brittle (leopard skin), Enlarged groin. Symptom of onchocerciasis reflects the developmental stage of the parasites and the degree of immune response by the host. Clinical manifestation are highly variable, however, symptoms do not appear until after the L3 larvae mature into adult worm. On average, symptoms appear between 9 months and 2 years after initial acquisition of the parasite and onset of symptoms is sometimes referred to as the prepatent phase.

**Diagnosis of onchocerciasis**

There are several test used to diagnose onchocerciasis, usually the first is for clinicians to feel the skin to try and identify nodules followed by laboratory studies which traditionally involves demonstration of microfilaria in a skin-snips biopsy sample. In this technique, a razor blade is used to remove tiny skin samples (3-5mg) from multiple sites, (iliac crest and shoulder). They are placed in saline to observe microfilaria emerging from the sample. Alternatively, for the purpose of quantification of microfilariae burden, sclerocone punch samples can be used to obtain a specific amount of skin (usually 5 micrograms) for each samples. The sensitivity is low in the prepatent disease stage, in geographic area of low prevalence and in areas of mass Ivermectin administration. Skin-snips biopsy spacers can also be used to detect microfilaria using nucleic acid amplification. This technique yield high specificity (100%) in experienced hands but low specificity (30-50%) in early stage of infection.
The diagnosis may also be made by direct examination of surgical specimens obtained by excision of nodules. Other methods entail the use of:

- **ov16 card test**: an immunochromatographic card test is used to detect the presence of immunoglobulin G4 (IgG4) antibodies to recombinant Ov16 antigen.
- **Recombinant hydride protein (ovh2 and ovh3)**: based on hybrid proteins of two separate onchocerca species (Ov₂₀ and Ov₃₀). An enzyme-linked immunoassay (ELISA) based antibody detection test.
- **An ELISA-based test using a cocktail of 3 antigens (Ov₇, Ov₁₁, Ov₁₆)** have been used to detect antibodies.
- **Test for low-molecular weight antigen fraction of formal Onchocerca volvulus parasites**.
- **Oncho-27 antigens test**: in the diagnosis of *Onchocerca* infection. The advantage of this test is the use of urine or tears for studying.
- **Nucleic acid amplification test**: Polymerase chain reaction (PCR) using materials from skin-snips or skin scratches provided high sensitivity and specificity superior to older methods. With the invention of Nucleic acid amplification test, Polymerase chain reaction (PCR), this has aid in early diagnosis of the disease as well as expression of the parasite genome.

**Other test**

An older techniques that is more of historical interest is the test dosing with Diethylcarbamazine (DEC) in oral form to observe the reaction that suggest the presence of onchocerciasis. More recently, a patch testing using Diethylcarbamazine which decrease risk have been used. This testing is based on the principle of the Mazzotti Reaction and involves the topical application of diethylcarbamazine in a cream base (DEC patch). It elicits localized cutaneous reaction (pruritis), maculopapular eruptions, etc.

**Treatment of onchocerciasis**

With the pathogenesis of onchocerciasis which is secondary to microfilaria, the goal of therapy is to eliminate the microfilaria stage of the disease to improve symptoms, prevent progression to eye lesions and to enhance disease elimination.

Therefore, World Health Organisation (WHO) recommends treating onchocerciasis with Ivermectin and Moxidectin as the drugs of choice due to it microfilaricidal property. Ivermectin is administered at least once yearly for dosing interval of 3-12 month for a period of 10-12 years. Where *Onchocerca volvulus* co-exist with loa loa, World Health Organisation recommends that treatment strategies be adjusted, since treatment of individuals with having high level of loa loa in the blood with Ivermectin can sometimes result in severe adverse events.

Recently, the approval of Moxidectin in June 2018 has also shown a promising progress toward combating onchocerciasis. Also, nodulectomy can result in cure if excision eliminates all adult worms. However, this is not a practical choice in patients with multiple nodules or in patients with whom nodules are not clinically evident.
Control and Elimination programmes

Due to significant human health and socioeconomic burdens associated with onchocerciasis, Onchocerciasis was identified by the World Health Organisation (WHO) as a potential candidate for disease elimination through annual or biannual mass administration of Ivermectin since 1970’s; an approach that has eliminated Onchocerciasis from all but four countries in America; reducing or eliminating the disease in many areas. With plans in place to gear-up for worldwide elimination by 2025, this has led to the establishment of several control programmes to enhance effective elimination of the disease ranging from; Onchocerciasis Control Programme (OCP); Following the dramatic consequences of onchocerciasis in West Africa, WHO launched in 1974 the OCP in collaboration with three other United Nations agencies including the World Bank, the United Nations Development Programme (UNDP) and Food and Agriculture Organization (FAO). These UN agencies constitute the sponsoring agencies of OCP. The programme stretched over 1 200 000 Km² to protect 30 million people in 11 countries, (Figure 6), from the debilitating effects of river blindness. For years, OCP operations were exclusively based on the spray of insecticides by helicopters and aircrafts over the breeding sites of the black flies in order to kill their larvae (aerial larviciding), (Figure 7). With the donation of Mectizan (ivermectin) by Merck and Co., Inc. in 1987, control operations changed from exclusive vector control to larviciding combined with ivermectin treatment or, in some areas, to ivermectin treatment alone. OCP was officially closed in December 2002 after virtually stopping the transmission of the disease in all the Participating Countries except Sierra Leone where operations were interrupted by a decade-long civil war.

Between 1974 and 2012, in West Africa using mainly the spraying of insecticides against black fly larvae (vector control) by airplane and helicopters. The Onchocerciasis Control Program (OCP) relieved over 40million people from the infection, prevented blindness in 600,000 people and ensured that 18 million children were born free from the threat of the disease and blindness. In addition, 25 million hectares of abandoned arable land were reclaimed for settlement and agricultural production capable of feeding 17 million people.

However, in 1995 experienced the lunched of the Africa Programme for Onchocerciasis Control (APOC), with the objective of controlling onchocerciasis in the remaining endemic countries in Africa and closed at the end of 2015. The APOC is a bigger partnership programme than OCP including 19 Participating Countries (Figure 8) with effective and active involvement of the Ministries of Health and their affected communities, several international and local NGDOs, the private sector (Merck and Co., Inc.), donor countries and UN agencies. The World Bank is the Fiscal Agent of the Programme and WHO is the Executing Agency of the Programme. The Community-Directed Treatment with Ivermectin (CDTI) is the delivery strategy of APOC. It empowers local communities to fight river blindness in their own villages, relieving suffering and slowing transmission. In Africa Programme for Onchocerciasis Control’s final year, more than 119 million people were treated with Ivermectin and many countries had greatly decreased morbidity associated with onchocerciasis. More than 800,000 people in Uganda and 120,000 people in Sudan no longer required Ivermectin by the end of 2015. Then, begins the transition into the Expanded Special Project for the Elimination of Neglected Tropical Disease in Africa (ESPEN). The establishment of the Expanded Special Project for the Elimination of Neglected Tropical Disease in Africa; with sustainable...
community-directed treatment with Ivermectin showed that as at 2016 to 2017, more than 132 million people were treated in Africa where the strategy of community-directed treatment with Ivermectin, (CDTI) was implemented, representing approximately 67.1% coverage of the number of people require treatment globally. The Expanded Special Project for the Elimination of Neglected Tropical Disease in Africa (ESPEN) like Onchocerciasis Control Program (OCP) and African Programmes for Onchocerciasis Control (APOC), is housed in the World Health Organisation (WHO) regional office for Africa and relies on support from priority countries for their neglected tropical disease programme. Also, in American, a similar program for the Americas known as the Onchocerciasis Elimination Program for the Americas, (OEPA) began in 1992 with it objectives of eliminating ocular morbidity and interruption of transmission throughout the America by 2015 through biannual large-scale treatment with Ivermectin. All 13 foci in this region achieved coverage of more than 85% in 2006, and transmission was interrupted in 11 of the 13 foci so far in 2017 with elimination effort now focused on the Yunomani people living in Brazil and Venezuela. Hence, several countries such as Colombia have been certified onchocerciasis free as at April, 2013 by WHO followed by Ecuador in September 2014, Mexico in July 2015 and Guatamela in July 2016 with more than 500,000 people no longer needing Ivermectin in the America.

National Policy on Onchocerciasis Control
The national health policy was introduced in 1988 to promote health for all Nigerians while a document containing the onchocerciasis policy as a national health intervention for the control of onchocerciasis as a priority disease was put forward in 2004. The ultimate goal is to eliminate onchocerciasis as a public health problem throughout Nigeria through strengthening of self-sustainable prevention and control programmes in endemic communities. The global target for the elimination of NTDs is 2025. The policy framework marked another milestone in the prevention and control of diseases that have greatly affected and incapacitated the productive and economically viable work force especially those that are predominantly farmers in the rural areas, remote villages and hinterlands. This informed the need for review of the progress made so far in order to transit from control to elimination and prevention to massive Ivermectin (Mectizan) and Albendazole administration to eligible individuals in endemic communities was introduced.

In 1988, the Federal Republic of Nigeria put up a National Health Policy, a strategy towards actualizing health for all Nigerians that represents the government and people collective will. However, implementing the framework has been more challenging. Health summit was organized in Nigeria in 1995 with the view for an urgent change in the health systems and status of the country. The Federal Ministry of Health (FMOH) responded to this and organized a review of the policy in 1996- 1997. The document was not endorsed officially then. It was endorsed and released as a policy blue print in September, 2004. The entire policy objective was, "To strengthen the national health system such that it will be able to provide effective, efficient quality, accessible and affordable health services that will improve the health status of Nigerians through the achievement of the health-related sustainable Development Goals.

The ministry of justice and other relevant ministries review priorities for health service and biomedical research, content of activities, promotion and financing of research activities and assessment of health technologies. They encourage private sectors collaboration in their activities that promote health and disease control. Research activities are predominantly targeted towards: biomedical and health services, operational research, developmental research, basic biomedical research which seeks to broaden basic knowledge relevant to biology and health; and research on socio-cultural factors which directly or indirectly affect health and

World Health Organisation (WHO) Policy on Onchocerciasis Control
In 1974, the World Health Organization (WHO) launched the Onchocerciasis Control Programme in Africa to combat the menace of river blindness in the region predominantly inhabited by farmers who are easily incapacitated by the scourge. The initial programme was predominantly via vector control by spreading insecticides along riverbanks to kill the larvae of Simulium. Merck and Co. Inc. further modified it in 1987 following ivermectin discovery. A combination of vector control and mass treatment using ivermectin was adopted. The control drive was enhanced to cover 19 countries of Africa from the previous 11 following the birth of The African Programme on Onchocerciasis Control (APOC). Their target was to treat 50 million people infested with filariasis annually by 2010 using free Ivermectin by Merck and Co. Inc. This was complimented by other programmes on training, research and development in tropical diseases by specialized United Nations Agencies, World Bank and World Health Organization (WHO). The African programme for onchocerciasis control was launched in 1995 to ensure wider coverage. It was targeted towards ivermectin distribution through Community Sustainable Distribution (CSD) approach. Following the elimination of microfilaricides, its use should be continued for 13–20 more years to ensure complete elimination in meso-endemic and hyper-endemic areas.

CONCLUSION
Overall, the results of this systematic review suggest that there have been a significant decrease in onchocerciasis infection in several regions of the country. However, the prevalence still persists mostly in river line area and regions which are inaccessible to the program as well as lack of orientation on the disease. Also, government policy on how often is ivermectin made available to the people and making provision to reach these areas yet covered and the decreased in larvae control have also contributed to the high prevalence of the disease in Nigeria. This accounts for the reason why over 40% of the world prevalence rate is from Nigeria.

Recent Advances in Diagnosis, Elimination and Treatment of Onchocerciasis
Several diagnostic methods have been recently discovered which involves:

- ov16 card test: an immunochromatographic card test is used to detect the presence of of immunoglobulin G4 (IgG4) antibodies to recombinant Ov16 antigen.
- Recombinant hydride protein (ovh2 and ovh3): based on hybrid proteins of two separate onchocerca species (Ov20 and Ov30). An enzyme-linked immunoassay (ELISA) based antibody detection test.
- An ELISA-based test using a cocktail of 3antigen (Ov2, Ov11, Ov16) have been used to detect antibodies.
- Test for low-molecular weight antigen fraction of formal Onchocerca volvulus parasites.
- Oncho-27 antigens test; in the diagnosis of onchocerca infection. The advantage of this test is the use of urine or tears for studying.
- Nucleic acid amplification test: Polymerase Chain Reaction (PCR) using materials from skin-snips or skin scratches provided high sensitivity and specificity superior to older methods. With the invention of Nucleic acid amplification test, Polymerase chain
reaction (PCR), this has aid in early diagnosis of the disease as well as expression of the parasite genome. 

Also, the recent approval of Moxidectin in June, 2018 has shown a promising progress toward combating onchocerciasis. The limitation on the use of Ivermectin in much central part of Africa owing to loa-loa coinfection as well as reliance on a single drug also increasing the potential for the emergence of Ivermectin-resistant *Onchocerca volvulus*, making development of new drugs or novel therapies imperative. Hence, there is the need for better study and understanding of the parasite. 

Due to the breeding habit of the vector and mode of infection, the need for a better understanding of the genome of this parasite; *Onchocerca volvulus*, cataloguing of possible nuclear and mitochondrial variants, as this will support future basic and translational onchocerciasis research with particular relevance for the ongoing onchocerciasis elimination program and boost efforts to characterise drugs, vaccines and diagnostic targets.

**ACKNOWLEDGEMENT**

We thank the management staffs of the University of Nigeria, Enugu Campus for their eminent help in making available resourceful materials which aid in ensuring the completion of this work. Also, we are grateful to Dr. Agada, Ali Samuel of the College of Health Science, Benue State University, Markurdi, Mr. Aondoaseer, Kaser and Mr. Avenger, Samuel U. of the Department of Medical Biochemistry, College of Medicine, University of Nigeria, Enugu Campus for their helpful decision and constructive comment on the Manuscript.

**CONFICT OF INTEREST**

The authors declare that there is no conflict of interest.

**ABBREVIATIONS**


**REFERENCES**


46. Centre for Disease Control (CDC). Onchocerciasis (also known as River blindness) prevention and control. Parasite. CDC. 2013. achieved from the original on April 2014.


