Vector-Borne Diseases & Treatment

Chapter 1

Filariasis: its Manifestations, Epidemiology and Control Strategies

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1. Introduction

Filariasis is a helminth disease, caused by parasitic worms known as filariae and transmitted through mosquito vectors. Filariasis presents a threat to public health as it causes severe long term disability and hampers one's socio economic status. Filariasis is endemic in many tropical and subtropical regions of the world. Lymphatic filariasis, a major type of the disease alone puts about 120 million people at risk of disease infection. When we trace back the history of the occurrence of this disease, though the first written document is from the Ancient Greek and Roman civilizations [1] yet the confirmation was made only many centuries later in 1877, when Sir Patrick Manson detected microfilaria causative agent of lymphatic Filariasis in mosquitoes. This was the first ever discovery of an arthropod acting as a vector of human diseases which was later found to be the case for other tropical diseases such as malaria, dengue *etc*. Even though it can affect individuals of all age groups and both genders, it is predominantly found to be associated with people of low socio economic status [2]. Moreover, filarial infection in general has been found to be more common in males than females. Although mortality is not associated with the disease, morbidity rate as a result of clinical manifestations is very high [3] and economic burden posed by the physical deformities resulting from infection have a severe psychological and socio economic impact [4].

A single bite of the infected vector does not establish the disease instead many years of continuous exposure to bites of hundreds of infected mosquitoes is required. This is because

inside the mosquito vector, multiplication of the filarial parasite does not occur. Approximately, 15,500 bites of infected *Culex quinquefasciatus* is essential for a new infection to occur [5].

2. Types

Depending on the site of occurrence of the parasite and the types of parasites causing the disease, filariasis has been found to be of four different types [1]. These are:

2.1. Lymphatic filariasis

Lymphatic filariasis is one of the most important neglected tropical diseases (NTDs) and is caused due to the infection with nematode parasites known as filarial worms. These worms belong to the Onchocercidae family and their infection results in the damage of one's lymphatic system. The causative agents of lymphatic filariasis are *Wuchereria bancrofti, Brugia malayi* and *B. timori*. About 90% of the infection is caused by *W. bancrofti* alone [6]. Although *Wuchereria bancrofti* and *Brugia malayi* live almost exclusively in humans, macaques and leaf monkeys in some parts of the world are said to be reservoirs of the parasites [1]. There is no other known natural animal reservoir of lymphatic filariasis, making man the only reservoir. Several species of mosquitoes serve as vector for these microfilarial worms. The vectors include *Culex quinquefasciatus, Anopheles gambiae, Aedes polynesiensis* and *Mansonia sp.* [7]. In many regions of Africa the *Anopheles* vectors of lymphatic filariasis is similar to those of malaria [8,9]. In Zambia, *An. funestus*, *An. gambiae* and *An. arabiensis* are the predominant species [10,11]. Periodicity of these microfilariae is directly related to the feeding habits of the above mentioned vectors. Almost all of these mosquito vectors feed during night hours except *Aedes polynesiensis*.

2.1.1. Transmission/life cycle

In 1877, Patrick Manson proposed that mosquito vector deposited microfilariae in water and human consumption of this contaminated water or direct skin penetration through contact led to the infection. However, it was George Carmichael Low who paved the correct mechanism of transmission of microfilariae in 1900 when he discovered the presence of pathogenic microfilariae in the mosquito's proboscis. When a mosquito bites an infected human, the microfilariae present in the circulating peripheral blood of human is also taken up by the mosquito vector along with the human blood. After 1-2 weeks of ingestion by the intermediate host, the microfilariae in the midgut of the vector shed their sheaths and make their way to the thoracic muscles. Here the microfilariae develop into first stage larvae, second stage larvae and finally to the third stage larvae which is also known as filariform larvae, which is infective to man. Then the third stage larvae migrate from the thoracic muscles of the vector to the proboscis through haemocoel. The infected vector introduces these larvae into a human host during another blood meal and larvae enter the body of the host through the bitten wound

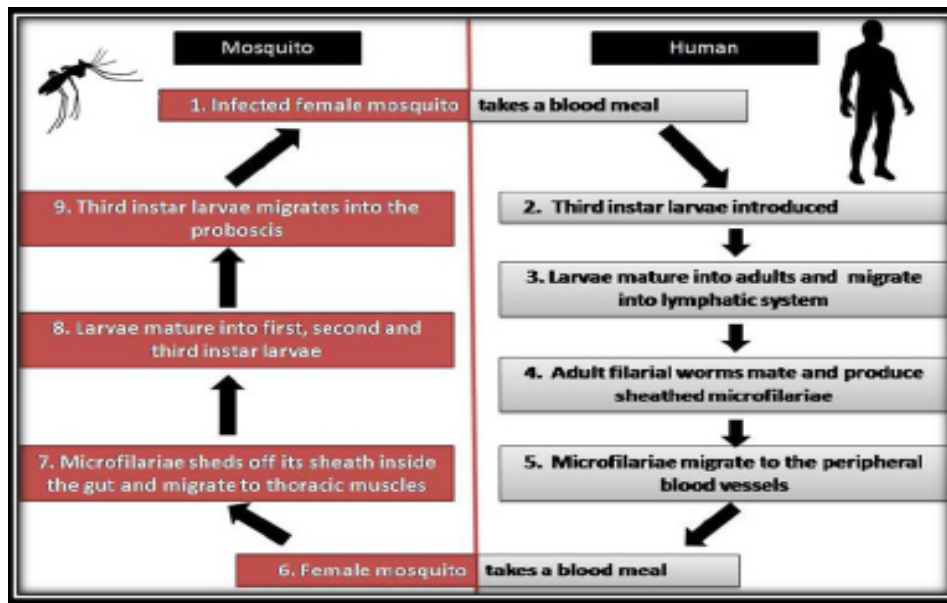and reach the lymph glands where they mature into adults.

Figure 1: life cycle of *Wuchereria bancrofti.*

This is a slow process and generally takes 5 to 8 months [12]. The mature male and female worms copulate to undergo sexual reproduction and produce sheathed eggs known as microfilariae. These circulate in the peripheral blood of the host in turn to be picked up by a mosquito and the cycle continues. Lifespan of adult worms is quite long and can live up to 10-15 years [1]. A mature female filarial nematode can produce microfilariae for up to about five years of maturation.

2.1.2. Symptoms

A light infection does not produce serious effects but causes filarial fever, headache and mental depression. A large number of pathological symptoms are observed during heavy infection of the parasites. Symptoms of lymphatic filariasis can be grouped into three categories such as asymptomatic infection, acute infection and chronic infection.

Asymptomatic infection*:* Some of the patients with lymphatic filariasis show no symptom of infection. Though these patients appear clinically asymptomatic, the parasites cause damage to the host's lymphatic system, kidneys and gradually alter the immune system.

Acute infection*:* In acute infection, microfilariae circulating in the human blood stream cause acute manifestation of lymphatic filariasis. The symptoms include episodic local inflammation of skin along with irregular and sporadic occurrence of lymphadenitis (*i.e.* inflammation of the lymph glands) and lymphangitis (*i.e.* inflammation of lymph channels), the latter two being characteristic of infection either by *W. bancrofti* or *B. malayi* [13]. Some of these inflammations are due to the action of host's immune response against the microfilarial parasites. Rest results from bacterial infection of the protective skin barrier of the host which becomes susceptible to such infections due to underlying lymphatic damage. During this

sporadic attack, the distal end of the affected limb of the host becomes swollen and may remain so for several days. In lymphadenitis, the parasites essentially take over lymph nodes in the body causing immune reaction and inflammation [14]. Inflammations related to acute infection results in immense pain and red streaks on the affected skin. Along with these symptoms, sometimes a patient may suffer from extreme pain in the genital area followed by formation of pus-filled nodules. These nodules keep on swelling until they rupture to discharge bacteria and dead adult worms.

Chronic infection: When adult worms deposit themselves in the lymphatic vessels and glands it results in lymphatic obstruction that restrains the back flow of lymph into the circulatory system. This results in the accumulation of lymph in the affected areas leading to enormous swelling in tissues of those areas thereby producing a condition known as lymphoedema [15]. But there are experimental evidences which propose that simple lymphatic blockage may not cause lymphoedema until and unless it is associated with certain inflammations. Later as infection increases there is invasion of plasma cells, eosinophils and macrophages resulting in chronic lymphatic damage and leakage of lymph into the tissues, thickening of the skin and underlying tissues and bacterial and fungal infections. All this leads to elephantiasis which is the most spectacular symptom of lymphatic filariasis and is more common in the lower limbs and genitalia than the upper extremities [1]. Elephantiasis due to the infection of *B. malayi* affects the upper and lower limbs with no genital pathology and infection with *B. timori* causes more swelling as compared to that of *B. malayi* and *W. bancrofti* [16]. Accumulation of fluid in scrotum and nearby areas of the host is termed as hydrocele and all types of scrotal enlargement due to the infection of microfilariae are termed as filaricele [17].In some cases, lymphatic blockage leads to the leakage of chyle and produce certain pathological conditions like chyluria, chylus diarrhoea and chylorrhagia [18].

2.2. Occult filariasis

Depending on whether or not the microfilariae can be found in the peripheral blood of the host, infected individuals may be termed as either microfilaraemic or amicrofilaraemic respectively. This amicrofilaraemic condition is termed as Occult filariasis. Though not found in the peripheral blood, microfilariae may be found in the tissues and other body fluids. Occult filariasis is believed to result from hypersensitivity reaction to filarial antigens. In a community where filariasis is endemic, only a small proportion of the population develops occult form of filariasis. The term occult filariasis embrace a number of pathological conditions such as, Tropical Pulmonary Eosinophilia (TPE), Glomurelopathies, filarial arthritis and filarial infections of the breast [19].

Tropical Pulmonary Eosinophilia (TPE) is the most common example of occult filariasis and is found mainly in the Indian subcontinent. It can be seen in people belonging to all

age groups and symptoms of the disease include cough, fever, chest pain, breathlessness and occasional abdominal pain. After infection, the microfilariae lodge in the lungs and pulmonary arteries of the host causing pulmonary lesions and is frequently accompanied by filariatic fever. TPE is characterized by high eosinophil level in the blood and asthma-like symptoms which is due to hyperresponsiveness of the host's immune system to the circulating microfilariae. If treatment is not provided for a long period of time the condition progresses to pulmonary fibrosis and respiratory insufficiency followed by impairment of lung function.

Glomerulopathies is associated with the production of typical lesions in the glomerulus and diffuse mesengial proliferation on the basement membrane. Filarial antibodies have been reported from patients with glomerulonephritis [20].

Filarial arthritis is usually common in the filariasis endemic areas and affects the knee joints. Though microfilariae may not be detected in the circulating fluid, however filarial antibodies may be detected in antibody test. It is important to differentiate filarial arthritis from rheumatoid arthritis as their respective treatment is quite different. The disease may be caused by other species excluding *W. bancrofti* [21]. In filarial arthritis, only the large joints are affected and majority of the patients have a painless swelling in the knees.

Filarial infections of the breast results in hard breast lumps attached to the overlying skin and at times are difficult to distinguish from malignant tumours [22]. Both adult worms and microfilariae have been found in the breast granuloma of patients through histological examinations.

The occult form of filariasis is generally caused by microfilariae but the symptoms are sometimes very much similar to other well known clinical conditions and are impossible to distinguish. The diagnosis of these occult manifestations can be done with ELISA test using specific antigens [19,23].

2.3 Onchocerciasis

Onchocerciasis also known as river blindness is caused by a parasitic microfilarial worm *Onchocerca volvulus*. It is also a NTD widespread in different countries of world. The parasite *O. volvulus* is transmitted by blackflies (*Simulium sp.*) that breed along fast flowing rivers and streams. An infected black fly introduces third stage filarial larvae into the human skin. The larvae then develop into adults and reside in the subcutaneous tissue nodules for up to 15 years. The adult worms produce microfilariae that migrate mostly to the skin and eyes. Symptoms include severe itching, disfiguring of the skin and eye lesions which sometimes can lead to permanent blindness [24]. Studies reveal that patients suffering from Chronic Onchocerciasis show increased eosinophil and high levels of serum immunoglobulin E (IgE) [1].

2.4 Loiasis

Loiasis also referred to as Loa loa filariasis is a skin and eye disease caused by a filarial nematode *Loa loa* commonly known as the African eye worm. The nematode is transmitted in human through the bites of deer flies or mango flies of the genus *Chrysops sp*. Two of the most important vectors include *Chrysops silicea* and *C. dimidiate* [25] that are generally found in the rain forest region of West and Central Africa. Adults harbour the subcutaneous tissue of the human host where the male and female mate and produce microfilariae that have diurnal periodicity probably due the day feeding habit of their vector. Clinical symptoms include localized swellings (popularly called Calabar swellings owing to the place of its first reported incident) most commonly in the limbs and rarely in the face. The adults often migrate into the eyes where it is externally visible for a short duration hence securing the name 'eye worm'. Loa loa infection generally does not affect normal vision but its movement through the tissues have been reported to be very painful [26,27]. Though infection with *L. loa* is usually asymptomatic microfilariae may sometimes be found in the blood, lungs, urine, spinal fluid and sputum [27].

In certain regions of West and Central Africa, loiasis is reported to be co-endemic with onchocerciasis. The first case was reported during the 1990s in Cameroon where patients with high intensity of Loa loa infection developed severe adverse neurological reactions after treatment with ivermectin for onchocerciasis [28,29]. This co-endemicity is of great concern because mass drug therapy for onchocerciasis with an anti-filarial drug ivermectin has an adverse effect on patients with high densities of Loa loa infection [28]. Probable explanation for the fore lying sentence is encephalopathy that results from massive killing of microfilariae near the optics and brain region in patients having high microfilarial loads [27]. Therefore, in communities with a high level of loiasis endemicity, there is a significant risk of severe adverse reactions to ivermectin treatment [30]. As a result, loiasis has recently evolved as an important public health issue.

3. Epidemiology

The World Health Organisation (WHO) considers lymphatic filariasis as one of the only six eradicable diseases and in order to achieve this goal proper information regarding disease prevalence should be considered. Lymphatic filariasis is endemic in tropical and sub tropical areas of the world and includes 32 of the world's 38 least developed countries [31,32] thereby developing a higher risk of infection to people living in those regions. Lymphatic filariasis endemic regions are Central Africa, Nile delta, Madagascar, Turkey, South East Asian countries, Thailand, Malaysia, Vietnam, South Korea, Indonesia, Philipines, Timor, Southern China, Guinea and Brazil [32,33]. Lymphatic filariasis affects approximately 120 million people in the world and 120 billion people are considered to be at a risk of becoming infected [34].

Approximately 15 million people with lymphatic filariasis live in Southeast Asian countries [35]. Earlier WHO estimated that on a global scale, a significant majority of filarial infections and disease cases occurred in India [36]. It was later reported that most number of cases around the world occurred in India (45.5 million) and Sub Saharan Africa (40 million) with India having 5% and Sub Saharan Africa having 8% of disease prevalence [34,37]. Sub Saharan Africa has the largest number of countries with moderate to high prevalence of filariasis and due to lack of current data on incidence of the disease in many of these countries, Sub Saharan Africa pose as the region where the disease is of immense public health significance [34]. Transmission efficiency of these diseases is also known to be higher in Africa than in Asia which may be due to the availability of different vectors that are responsible for transmission of filarial worm in these two distinct geographical locations [37]. In general, *Anopheles sp.* transmits the disease much more efficiently than *Culex sp.*, although with a few exception [38].

Infection with *Onchocerca volvulus* is prevalent mainly in the tropical areas. Though most of the infected people are found living in 31 countries of sub-Saharan Africa [39], occasional reports on cases with onchocerciasis have also come to the limelight from Yemen and the United states.

Loiasis is an African disease that is restricted to the rain forest region of West and Central Africa [30,40,41] limiting its distribution to Benin in the West, Uganda in the East and Zambia towards the South [42]. Highly endemic regions for loiasis are the Equatorial Guinea, Gabon, Cameroon, Democratic Republic of Congo, Central African Republic, Chad and Sudan [30]. Endemicity of the disease is closely linked to the habitats of its vectors *Chrysops silicea* and *C. dimidiate*. An estimated 12-13 million people in the endemic area are disease affected [43]. As co-endemicity of loiasis with Onchocerciasis possesses a great hurdle towards control of filariasis, knowledge relating to the co-endemic regions is important. Loiasis was once prevalent in Ghana, Mali and Ivory Coast but has now been completely and successfully eradicated [43]. Cases of Loa loa infection have also been occasionally reported from the United States but only in those who have returned from endemic areas [43-45].

4. Diagnosis

For implementation of effective control programs at community levels, an accurate diagnosis of filariasis should be of prime concern. The first and foremost step involves collection of information regarding the exposure of patient in endemic areas whether currently or in the past and thereafter laboratory tests can be carried out like:

i.   Serology test to detect circulating microfilariae in the peripheral blood. However, the periodicity of the pathogen should be kept in mind [46]. This is by far the most widely used diagnostic technique due to its simplicity and low cost.

ii.   For detection of *Onchocerca volvulus,* skin biopsy is usually performed.

iii.   PCR tests using species-specific primers to detect DNA of the pathogen in human blood and also in the infected vector.

iv.   Immunochromatographic test holds advantage in being independent of periodicity of the pathogen [47].

v.   Ultrasonography to locate filarial worms in the genitals of asymptomatic males. This is a prime diagnostic technique to distinguish between cases requiring immediate surgery and cases that can be dealt with drugs [17].

Recently, many advanced techniques and methodologies have been developed for the diagnosis off ilariasis worldwide like filariasis strip test [48,49], antibody rapid test, molecular xenomonitoring to detect filarial DNA using reverse transcriptase PCR (RT-PCR) and loop mediated isothermal amplification for rapid detection of filarial DNA in mosquitoes [50,51].

5. Anaphylactic Treatments

5.1 Drug therapy

Several drugs are used for the treatment of filariatic infection. Most important and the commonly used ones are Diethylcarbamazine (DEC), Ivermectin, Suramin, Albendazole, Mebendazole, Flubendazole and Doxycycline [1]. DEC is both micro-filaricidal and macro-filaricidal thereby being a drug of choice for patients with active Lymphatic filariasis. It is a potent micro-filaricidal drug and also has moderate macro-filaricidal effect [52]. The most important action of DEC appears to be the alteration of microfilariae, which are readily phagocytosed by tissue fixed monocytes but not by the circulating phagocytes [53].Recommended dose for DEC is 6mg per kg body weight per day for 12 days [37]. However, recent studies also report that a single dose of DEC (300 mg) in combination with albendazole (400 mg) is equally effective [54]. Ivermectin and Suramin are efficient only against microfilariae and not the adult worms. The filarial nematodes when exposed to these two drugs develop tonic paralysis. Ivermectin can be used to treat onchocerciasis but has to be administered only in areas where co-endemicity of loiasis does not occur as the drug has an adverse effect on patients infected with high intensities of Loa loa infection [55]. Studies show that Albendazole works by decreasing the ATP production in worms thereby resulting in energy depletion, immobilization and death of the filarial worm [56,57]. Albendazole can also be used in combination with DEC and Ivermectin to increase the anti-helmintic property [58]. The combination of Albendazole with DEC and Ivermectin has shown to reduce the prevalence of angioedema in a study conducted in South India [59], and the same in Nigeria has shown to reduce mosquito infection rates [60]. The triple drug combination of Albendazole, DEC and Ivermectin represents a potentiality

to significantly reduce the number of doses of anti-helmintic drugs when used singly [61]. Mebendazole and Flubendazole acts by blocking the glucose uptake of nematodes. This results in glycogen depletion and reduced ATP generation but the blood glucose levels of the infected human remains unaffected. Doxycycline is a drug that ultimately hampers the embryogenesis of the filarial nematode [62] leading to sterilization or reduced reproduction, but is used not directly against the nematode but against its endo-symbiont a bacteria *Wolbachia*. Doxycycline, alike Ivermectin can also be administered in Onchocerciasis and loiasis co-endemic areas. Ivermectin is also contradicted among pregnant women, nursing mothers and small children [63].

Hydrocele can be treated by frequent excision of the overlying skin following the traditional procedures and thorough cleaning of the skin. Surgical treatment for lymphoedema of the limb can be of two major types *i.e.* drainage and excision. In drainage procedure the lymph flow of the infected individual is improved by either bypassing the blocked portion or addition of new lymph channels. Excisional procedure is the trimming off of the extra large limb volume.

Herbal treatments: For centuries, people used and still use several herbs against filarial infection. Some of the herbs being used for treatment of filariasis in South Africa are *Elephantorrhiza elephantine, Eucomis autumnalis, Ganoderma sp., Solanum aculeastrum, Hermannia geniculata, Datura stramonium, Ricinus communis* and *Pentanisia prunelloides* [64].These herbs can be used individually or in a combination to enhance their effect against the disease. Some of the herbs like *Vitex negundo, Butea monosperm a*and *Aegle marmelos* have also been reported to show antifilarial activities [65].

5.2 Targeting Wolbachia an endosymbiont of filarial nematodes

Wolbachia, a gram-negative proteobacterium is an endosymbiont in all human filariae belonging to family Onchocercidae except *Loa loa* [66,67]. Studies on the symbiotic relationship between *Wolbachia* and Onchocercidae show that *Wolbachia* promotes normal development, fertility and survival in the filarial worm. Till date, relationship between *Wolbachia* and Onchocercidae is considered to be mutualistic [68] as evident from the complete genome analysis of *Wolbachia* in *Brugia malayi* [69]. The bacterium is vertically transmitted to the filarial progeny through the female germline [70]. *Wolbachia* till now has not been detected in any other nematode groups [71,72] excluding Onchocercidae [73].

On contrary to the endosymbiont nature of *Wolbachia* in Onchocercidae, this bacterium is highly parasitic in arthropods. As a result, in mosquitoes, it inhibits the transmission of certain viruses like Dengue, Chikungunya, Yellow fever, West Nile and also of malarial parasite *Plasmodium* and filarial nematodes [74].

Most anti-filarial drugs currently in use are effective only against the larval forms of filariae, *i.e.* microfilariae and development of resistance against those has also been reported [74]. The adult worms can survive in the human host for 10-15 years and has the ability to fecund for almost their entire lifetime. Keeping this in mind drugs must be administered for a long period of time. Targeting the adult worm is the need of the hour. This can be achieved through targeting *Wolbachia* whose depletion may in turn result in stunted embryogenesis [62] and death of the adult worm.

Wolbachia is present in all larval stages of filarial nematode and also in the adults [75,76] being mainly localized in the hypodermal cells [77]. It is also found in the ovaries and uterus of the female but has never been reported in the male reproductive system [78]. *Wolbachia* plays an important role in triggering pro-inflammatory response in the patient and also enhances the survival rate of the nematode. Therefore, targeting *Wolbachia* as a filaricidal seems to hold great potentiality for treatment of filariasis. Doxycycline has already been recommended as an anti-Wolbachia therapy for the treatment of lymphatic filariasis and onchocerciasis [79,80].

Electron microscopy study has shown the absence of *Wolbachia* in microfilariae [81,82] and adults of *Loa loa*[83], this has further been confirmed by PCR analysis. Agreeing to which Helen *et al.,* reports that the neurological consequences following ivermectin treatment of individuals with *Loa loa* are not associated with *Wolbachia* [82]. In co-infected individuals, post treatment reactions may be due to adverse events induced by *Wolbachia* derived from either *O. volvulus* or *W. bancrofti* [82].

6. Control and Prevention of Filariasis

The principal approach in community control of filariasis is the mass administration of anti-filarial drugs known as Mass Drug Administration (MDA) in the endemic areas. MDA consists of annual or semi-annual drug administration initially for 4-5 years. The use of anti-Wolbachia drug doxycycline may also be considered for MDA but as the required treatment course being six weeks, makes its large scale implementation very difficult [84].

Secondarily, focus has to be made on vector control strategies in order to sustain the advantages of MDA. Lack of vaccine against filariasis makes vector control and management through insecticides, one of its prime strategies to eradicate the disease. However, the widespread developments of insecticide resistance in vector populations pose a great threat to vector control. Moreover, prolonged vector control, do contribute to subsidence of parasite transmission though recently it is widely accepted that vector control should complement chemotherapy [85]. Vector control when used with DEC administration reduced transmission rate significantly when compared to drug administration alone [86]. Studies in Tanzania and India have reported reduced transmission through the use of vector control strategies. The use of insecticide treated bed nets (ITNs) or long lasting insecticide treated bed nets (LLINs) and

untreated nets in combination with chemotherapy has documented a reduction in prevalence of lymphatic filariasis in countries like Kenya, Nigeria and Papua New Guinea [86-87]. Senkwe *et al.,* reported a significant decline in lymphatic filariasis when use of ITN scaled up through the entire nation in Zambia [88]. Habitat destruction of the vector has also been one of the targeted steps. Application of insecticides and biological agent *Bacillus thuringiensis israeliensis* in the breeding grounds of the vectors help control vector population to some extent. As man is the only host of *Wuchereria bancrofti*, its transmission can be interrupted efficiently by implementation of MDA and vector control strategies.

6.1 Control programmes worldwide

In the year 2000, the Global Programme to Eliminate Lymphatic Filariasis (GPELF) was launched by World Health Organisation (WHO) with a prime objective to interrupt transmission of the parasite [89]. GPELF aims to eliminate lymphatic filariasis as a public health problem by 2020 through two strategies mentioned below.

i. Interrupt the transmission of disease following four sequential steps.

a. Mapping areas to determine the geographical distribution of the disease and identify endemic areas.

b. MDA is then implemented to the entire populations living in the disease endemic areas. It includes single dose of DEC or ivermectin combined with albendazole initially for a period of five years to the populations at risks.

c. After the end of MDA programme, infection levels are monitored through post-MDA surveillance of the endemic areas in order to identify areas of ongoing transmission.

d. Verification of the absence of transmission is the final step to check whether a country succeeded in interrupting transmission or not.

ii. Reduce suffering and disability of the infected people by introducing measures ike improved hygiene and skin care for lymphoedema patients and provision of surgery for hydrocele patients. Morbidity management is considered as an integral step in the eradication of lymphatic filariasis. Therefore, managing mobidity to relieve sufferings related to the disease is one of the primary motive of GPELF. Morbidity management basically includes providing lymphoedema management, urogenital surgery for affected males, improving hygiene and skin care on the affected portion and to promote improvements in the quality of life of people infected with lymphatic filariasis.

After the launch of GPELF, the rate of mass distribution of anti-filarial drugs significantly rose up. During the first 10 years, the number of people treated by MDA increased from 3

million in 12 countries in 2000, to 466 million in 53 countries in 2010 [90] but the efforts to provide mobidity management was not up to the mark. WHO then recommended the preventive chemotherapy and transmission control as a primary strategy to interrupt the transmission of lymphatic filariasis. Preventive chemotherapy is executed through MDA in the endemic areas and transmission control approach focuses on vector control techniques.

Along with MDA and vector control, emphasis should also be given to improve water quality, sanitation, hygiene and general living standard [91]. As an alternative strategy, WHO has now launched water, sanitation and hygiene (WASH) campaigns for interrupting the transmission of the parasite. Through sanitation campaigns against *Culex quinquefasciatus*, lymphatic filariasis has been eliminated from Australia and reduced significantly in many parts of Brazil [92].

As mentioned earlier, WHO has recommended the following four steps that should be followed in order to make the Filariasis elimination campaign fruitful.
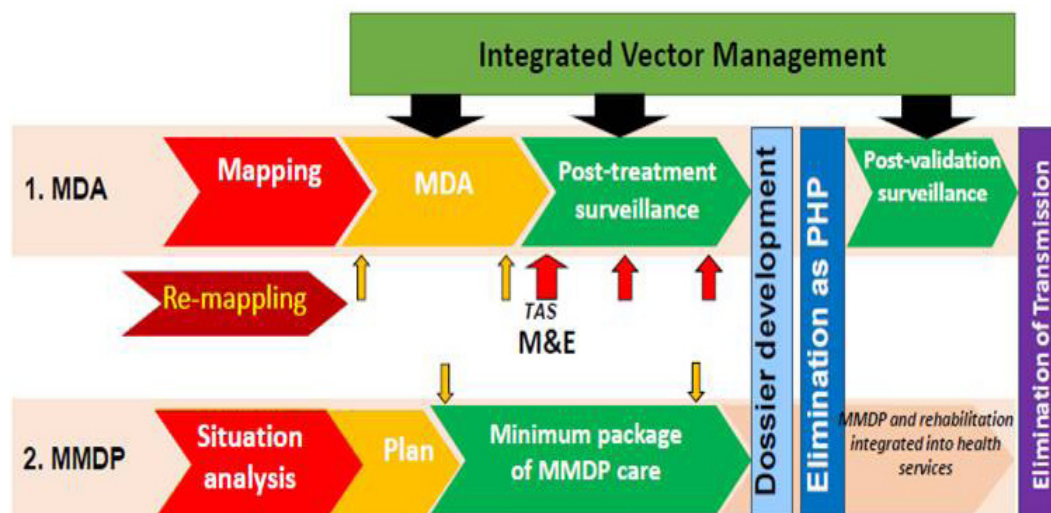
a.   Mapping the area to determine the geographical distribution of the disease.

b.   MDA initially for 5 years and thereafter decision should be made whether to stop MDA or not based on the researches carried out on the recent transmission rate of the disease.

c.   The area should be kept under surveillance even after completion of MDA.

d.   Decrease in transmission rate should be checked during short time intervals.

In 2012, many organizations from around the world joined together against NTDs and signed the London Declaration with the aim to control and eradicate the NTDs. Since then, lymphatic filariasis has been targeted to be eliminated from the world by 2020 [51]. To achieve this goal, in combination with the various strategies earlier mentioned in this chapter, increase in funding and donations from government and other organizations are equally important.

Control of onchocerciasis is executed with the help of three programs in Africa, West Africa and the Americas [39]. In Africa, from 1995-2015, the African Program for Onchocerciasis Control (APOC) was implemented and mainly focused in controlling onchocerciasis through sustainable community-directed treatment with an anti-filarial drug ivermectin. It also supported the vector control program using environmentally safe methods. APOC in Africa has now been replaced by the Expanded Special Project for the Elimination of Neglected Tropical Diseases (ESPEN).

In West Africa, onchocerciasis has been brought under control by the WHO Onchocerciasis Control Program (OCP). This program mainly focuses on the vector control strategies through use of insecticides against the black flies supplemented by MDA of ivermectin in the endemic regions. The Onchocerciasis Elimination Program of the Americas (OEPA) operated through MDA with ivermectin twice a year. All of the combined effort against the disease led to the eradication of onchocerciasis first from Colombia (2013) then followed by Ecuador (2014), Mexico (2015) and Guatemala (2016).

7. Conclusion

Lymphatic filariasis and onchocerciasis forms a major portion of NTDs in tropical and subtropical countries. Though steps both at the community level and global level have been implemented for successful eradication of these diseases, yet they still persist and seriously affect the socio-economic status of a country. Along with the therapeutic treatment, much importance should be provided to the follow up thereafter to prevent related secondary infections. In lymphatic filariasis, avoidance of secondary bacterial and fungal infection in the affected portion of the patient is a must for proper management of the disease. Much scientific studies should be directed to Loiasis, which has recently come into focus because of the hindrance provided by its causative agent in the MDA against onchocerciasis with ivermectin. Eradication steps therefore, should also involve ways to tackle such associated problems through improving the current tools and techniques and the methods of assessment. Vector control is a promising tool against filariasis and also other vector borne diseases. Prior information regarding insecticide resistance status and the degree of resistance towards a particular group of insecticides has to be in mind before the application of an insecticide against a vector. Survey of the endemic areas and research relating to insecticide susceptibility/resistance status of different vectors provides a baseline data for designing of an efficient vector control program. Therefore, such surveys and researches should be encouraged and promoted at the regional levels. Lastly, the involvement of mass/community should be encouraged for the efficient implementation as well as proper management for the eradication for the eradication of these diseases.

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