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Neglected parasitic infections (NPIs) of tropical countries: current status and control strategies

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Abstract

Neglected Parasitic infections (NPIs) are group of parasitic infections which are common in low income populations those who struggle to meet their daily basic needs and inaccessibility of primary health care services. The reason behind NPI's are may be poor population with low visibility and little political voice and also may be due to the lack of awareness of clinician and poor availability of optimal diagnostic tests. Confirmatory diagnosis of these parasitic infections requires well established lab, reagents, advance diagnostic methods. Therefore, there is an urgent need to develop improved diagnostic methods. According to recent report of World Health Organization (WHO) there is salient achievements related to decrease in number of new cases of certain disease including Visceral Leishmaniasis (VL), Lymphatic filariasis (LF), Human African Trypanosomiasis (HAT), Oncocerciasis by implementation of proper control strategies including preventive chemotherapy, innovative and intensified disease management, vector ecology and management, veterinary public health services, and the provision of safe water, sanitation and hygiene.

Keywords: NPIs, VL, HAT, LF, WHO

1. Introduction

Parasitic infections are major global health problem. The neglected parasitic diseases are group of parasitic infections which are common in low income populations in developing countries of Africa, Asia, and America ^[1]. These parasitic infections are acquired in their own immediate environment where substandard housing, lack of access to safe water and sanitation, chronic hunger, filthy environments, close contact vectors, domestic animals and livestock contribute to their efficient transmission. They are caused by helminths and protozoa. These infections are unlike other emerging diseases (TB, Malaria and HIV) which are not receive greater attention in terms of treatment and research funding by policy makers and public and private stakeholders ^[2]. Disease primarily occurs in world's poorest people who live on less than US\$2/day or below the World Bank poverty figure of US\$ 1.25/day ^[3, 4]. WHO identified 17 tropical diseases as neglected including 11 neglected parasitic infections (NPIs). Major NPIs caused by Helminths are Dracunculiasis, Echinococcosis, Fascioliasis, Lymphatic filariasis, Onchocerciasis, Schistosomiasis, Soil-transmitted helminthiasis (Ancylostomiasis, Ascariasis, Trichuriasis), Cysticercosis/ Taeniasis, Food born trematodiasis (Fasciolosis, Fasciolpsis, Paragonimiasis, Clonorchiasis) and Protozoa are African Trypanosomiasis, Leishmaniasis ^[5, 6]. These NPI's share a key characteristics, including i) large number of peoples are affected especially poor population with low visibility and little political voice; ii) lack of awareness of clinician and poor availability of optimal diagnostic tests leads to underreporting and missed diagnosis of diseases, iii) Can be controlled, prevented and possibly eliminated using effective and feasible solutions ^[7, 8]. This review mainly focuses on current status of neglected parasitic infection in and around the world and salient achievements result from the implementation of the proper control strategies recommended by World Health Organization.

2. Neglected Parasitic Infections

2.1 Leishmaniasis

Visceral leishmaniasis (VL) is the most serious form of the disease, also known as Kala-azar. It is endemic in more than 80 countries, predominantly rural disease caused by *Leishmania* protozoan parasites are transmitted through the bites of infected female *Phlebotomus* (sandflies) ^[9,10].

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Three main forms of the disease are visceral, cutaneous and mucocutaneous ^[11]. Disease is prevalent in 88 countries on 4 continents and highly endemic in the Indian subcontinent and in East Africa, where an estimated 2, 00,000 – 4, 00,000 new cases reported each year. According to WHO ^[12] total 30,758 cases in 2014 and 21,909 cases in 2015 of VL whereas total 1,53,027 cases in 2014 and 1,38, 575 cases in 2015 of cutaneous disease have been reported. About 90% of VL cases have been reported from Bangladesh, Brazil, Ethiopia, India, Nepal and Sudan, about 90% of cutaneous leishmaniasis cases occur in Afghanistan, Algeria, Brazil, Peru, Saudi Arabia, Sudan, the Islamic Republic of Iran and the Syrian Arab Republic and about 90% mucocutaneous leishmaniasis cases occur in Brazil, Peru and the Plurinational State of Bolivia ^[11,12,13]. Bangladesh, India and Nepal, which have the highest burden of visceral leishmaniasis, have decided to reduce the incidence to less than 1 case/10,000 individuals by 2015 ^[13]. In 2012, the WHO Roadmap ^[14] on neglected tropical diseases targeted regional elimination of visceral leishmaniasis by 2020. Substantial progress has been made the incidence of reported new cases decreased by around 67% (Bangladesh), 61% (India) and 46% (Nepal) in 2015 ^[13].

According to WHO report ^[13], there is a significant increase in elimination target in Bangladesh and India from, 90% and 67% in 2014 to 97% and 82% in 2015, respectively. In 2016 Bangladesh reached the elimination target 99% and India 85%. In India adoption of newly developed liposomal Amphotericin B was highly effective, it has almost no side-effects and as first-line treatment in 2014 and it is a major factor in progress towards eliminating visceral leishmaniasis from India. This medicine was donated through WHO by Gilead Sciences and around 66% of total number of kala-azar cases treated ^[13]. In order to control and elimination of visceral leishmaniasis in the Indian subcontinent, WHO has signed a new five-year agreement with Gilead Sciences that extends there donation up to 2021.

2.2 Chagas disease (American trypanosomiasis)

Chagas is a chronic parasitic infection caused by flagellated protozoan parasites *T. cruzi*, transmitted by faeces of triatomine bugs ^[9, 15]. About 6–7 million people worldwide are estimated to be infected, mainly in endemic areas of 21 Latin American countries: Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, French Guiana, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Uruguay, and Venezuela. 75 million people at risk of infection ^[13].

2.3 Sleeping sickness or Human African trypanosomiasis (HAT)

Human African trypanosomiasis is caused by flagellate protozoa ^[16], *Trypanosoma brucei gambiense* (chronic form) or *Trypanosoma brucei rhodesiense* (acute form) is found in remote Sub-Saharan areas where health systems are often weak. *T. b. gambiense* is endemic in 24 countries of west and central Africa and more than 90% of cases have been reported ^[11]. Between 1999 and 2008, the reported number of cases of the chronic form of human African trypanosomiasis (*T. b. gambiense*) decreased by 62%, from 27,862 to 10,372 and the acute form of human African trypanosomiasis (*T. b. rhodesiense*) decreased by 58%, from 619 to 259. Since 2005, there is reductions occurred in the numbers of new cases of human African trypanosomiasis by 89% in 2015 ^[13].

2.4 Lymphatic Filariasis

It is commonly known as elephantiasis. It is caused by the nematode worm, either *Wuchereria bancrofti* and *Brugia malayi*, transmitted by vector mosquito ^[9, 17, 18]. About 90% of infections are caused by *Wuchereria bancrofti*, 9.9% by *Brugia malayi* and remaining (0.1%) by *Brugia timori* ^[19]. It is a disfiguring and disabling disease, which is generally acquired in childhood ^[20]. The lymphatic system is damaged. Infected persons sustain the transmission of the disease. The long term physical consequences are painful swollen limbs (lymphoedema or elephantiasis). Hydrocele in males is also common in endemic areas ^[17].

Lymphatic filariasis is endemic in 81 countries ^[13]. WHO estimates total 947 million people in 54 countries worldwide remain threatened by lymphatic filariasis and requires preventive chemotherapy to stop the transmission of this parasitic infection. India contributes about 40% of the estimated cases globally with either disease or infection (microfilaria cases) ^[13]. In 1995 National Filarial Control Programme (NFCP) was launched by India it is a part of the National Vector Borne Disease Control Programme (NVBDCP) through which World Health Assembly targets to eliminate the disease by 2020 ^[13].

Progress and Achievement against LF

In India the population coverage during mass drug administration has improved from 73% in 2004 to 89% in 2015 which has resulted in the overall reduction of microfilaria rate from 1.2% in 2004 to 0.3% in 2015 ^[13]. According to recent report of National Vector Borne Diseases Control Programme (NVBDCP) of the Union health ministry, Out of 250 districts (now 255 due to division of old districts), 203 have reported overall microfilaria rate of less than 1%. Ministry official said that India is now on the verge of reaching elimination targets nationally". "After receiving polio-free certification in 2014 now India prepare for next public health success story of eliminating filariasis. Globally, 351 million people no longer require preventive chemotherapy due to successful implementation of WHO strategies by 2015 ^[13].

2.5 Soil-transmitted helminthiasis (STH)

Soil transmitted helminthes affect nearly 15 billion people mainly children's. ^[21]. Soil-transmitted helminthiasis (especially hookworm) are harmful to the health of pregnant woman as well as their child they mainly cause iron deficiency and anemia ^[5, 21, 22]. Lack of access to safe/clean water and proper sanitation is the main factors in the persistence and prevalence of the disease. According to the World Health Organization estimates, 870 million children live in the area of high prevalence of soil transmitted disease. The latest estimates for 2014 indicate that approximately 1.5 billion people are infected with soil-transmitted helminths worldwide ^[23]. Infections are widely distributed in tropical and subtropical areas; most occur in sub-Saharan Africa, the Americas, China and South-East Asia ^[24]. South Asia include three soil transmitted helminth infections, ie. Ascariasis, Trichuriasis, and Hookworm infection. India alone contributes nearly 25% to the total global cases with 220.6 million children in need of preventive chemotherapy ^[13]. Soil-transmitted infections cause the loss of an estimated 3.39 DALYs (Disability adjusted life year). Asia accounts for about 70% Global health estimates ^[13]. In India the overall prevalence of STH was in range 7.56 to 78.27%. The

prevalence of *Ascaris lumbricoides*, *Anchylostoma duodenale* and *Trichuris trichura* in these studies was in range between 0.4 to 71.87%, 0.14 to 42% and 0.3 to 29.57%, respectively. Most studies 17 (94.4%) revealed multiple infection [23]. *Ascaris lumbricoides* was the most prevalent parasite from 19 different states. Higher than 50% prevalence were reported from six states. Nearly 90% studies reported the prevalence of more than one parasite species in the same sample population. [25].

2.6 Food borne trematode infections

It is a group of parasitic infections caused by trematodes (flatworms or “flukes”) including Clonorchis, Opisthorchis, Fasciola, Fasciolopsis and Paragonimus that are acquired through ingestion of food contaminated with the larval stages of the parasite [26]. Transmission mainly depends on methods of producing, processing and preparing foods. In some area dishes containing raw fish, crustaceans and plants are dietary tradition of many populations. It affects millions of people, mainly in Asia. The public-health significance of these infections is gaining recognition. All of them cause significant morbidity, while Clonorchiasis and Opisthorchiasis lead to cholangiocarcinoma and death if left untreated. [26]. Fascioliasis globally reported from more than 70 countries in Asia and Latin America worldwide [26]. In 2005, more than 56 million individuals were infected with food borne trematodes in 17 countries, among them 7.9 million people suffered severely and more than 7000 died [27]. Recently in 2015 *Faciolopsis buski* case reported from Bihar [28]. In India, several case of *Faciolopsis buski* has been reported with high prevalence from Assam, Uttar Pradesh and Maharashtra [29, 30] and also sporadic cases have been reported from Bihar, West Bengal, Manipur, Odisha, Tamil Nadu and Karnataka [31, 32].

2.7 Neurocysticercosis

Neurocysticercosis is fatal parasitic disease which is caused by larval stages of *Taenia solium* (*Cysticercus cellulosae*) after consuming food and water contaminated with eggs [33, 34]. Neurocysticercosis occurs when cysts formed within the brain causing neurologic syndromes such as epileptic seizures [35]. It has been called a “hidden epidemic” [36]. More than 80% of the world’s 50 million people with epilepsy live in developing countries. Neurocysticercosis is responsible for 20% to 50% of late-onset epilepsy cases globally. It is also reported to be a common cause of juvenile epilepsy in certain countries, like India and South Africa [36]. WHO estimates the *T. solium*, cause 28, 000 deaths per year and 2.8 million DALYs globally [13]. Human cysticercosis has not been eliminated from any region of the world by any specific control programme because there is no national surveillance and control programmes in place anywhere in the world, except in China [37].

2.8 Echinococcosis

Echinococcosis is a parasitic disease caused by tapeworms of the *Echinococcus* type. There are two main types of the disease one is *cystic echinococcosis* and another one *alveolar echinococcosis* [38]. Transmission occurs through ingestion of food or water that contains the eggs of the parasite. It has a global distribution, and causes serious morbidity and death if untreated [38, 39]. Cystic echinococcosis is endemic in Bangladesh, Bhutan, India and Nepal, and causes disease in livestock and people [40]. It is recorded that approximately 200,000 new cases are diagnosed annually. The highly

endemic areas are the Eastern Mediterranean Region, northern Africa, southern and Eastern Europe, South America, and Central Asia, Siberia and western China [40]. It estimated that more than 19 000 deaths per year and around 870 000 disability-adjusted life-years globally [41]. Cystic echinococcosis also imposes a significant economic burden in developing countries by affecting livestock, causing an estimated US\$ 2 billion in livestock losses alone. The economic losses due to Cystic echinococcosis of the livestock and human in India was first time systematically analyzed by Singh *et al.* [42] analysis reveal that total annual median loss of Rs. 11.47 billion (approx. US \$ 212.35million). Cattle and buffalo industry accounted for most of the losses: 93.05% and 88.88% of the animal and total losses, respectively. Human hydatidosis related losses were estimated to be Rs. 472.72 million.

2.9 Schistosomiasis

Also known as snail fever and Bilharziasis a parasitic disease caused by flatworm *Schistosoma* spp. Parasite affects urinary tract and intestinal tract and symptoms include abdominal pain, diarrhoea, bloody stool, or blood in the urine [20]. In India the prevalence of it varied from 2.1% and 12.5% during the year with highest infection rate during winter and the rainy season [43]. According to WHO report, in 2008, 17.5 million people were treated for schistosomiasis globally while in 2015, a total of 74.3 million people received preventive chemotherapy for schistosomiasis it representing coverage of 31% [13].

2.10 Dracunculiasis

Dracunculiasis (Guinea worm) infection caused by *Dracunculus medinensis* round worm. Disease was widespread at the beginning of the 20th century, but during the 1980s transmission was limited to 20 countries of WHO’s African, Eastern Mediterranean and South-East Asia regions [44]. By the end of 2009, only four countries (Ethiopia, Ghana, Mali and Sudan) had cases, Sudan alone accounted for 86% of all cases [45]. Dracunculiasis is on the verge of eradication. In 2016, only 25 human cases have been reported. This achievement will make it the second infectious disease to be eradicated after smallpox. Certification of India as a Guinea Worm disease free country by the World Health Organisation in February 2000 is a major success story of disease eradication in India [13].

2.11 Onchocerciasis (River blindness)

Onchocerciasis is a disease caused by infection with the parasitic worm *Onchocerca volvulus*. The parasite worm is spread by the bites of a black fly of the *Simulium* spp [9, 46]. More than 99% of people infected with *O. volvulus* live in 30 endemic countries in the African Region; the remainder lives in Yemen and 6 countries of the Region of the Americas [47]. About 15.5 million people are infected with river blindness. Approximately 0.8 million having loss of vision from this infection [48]. In 2015, more than 114 million people were treated in in Africa. Colombia was the first country in the world to be declared as Onchocerciasis free country by WHO on 5 April 2013. This has been followed by Ecuador in September 2014, Mexico in July 2015, and Guatemala in July 2016 [13].

3. Achievements for control of Neglected Parasitic Infection

These achievements result from the implementation of the five interventions recommended by WHO to overcome NTDs, namely: preventive chemotherapy, innovative and intensified disease management, vector ecology and management, veterinary public health services, and the provision of safe water, sanitation and hygiene^[13].

- In 2015, 557.9 million people received treatment for lymphatic filariasis. This is the highest rate of treatment coverage of 59.3%.
- In 2015, 119 million people received Ivermectin treatment for onchocerciasis, representing 64.1% coverage.
- In 2015, Human African trypanosomiasis case has been reduced by 89%.
- In Bangladesh, India and Nepal, Visceral leishmaniasis cases has been reduced by 82%.
- In 2017 the 10th meeting of the Strategic and Technical Advisory Group for Neglected Tropical Diseases received proposals for the addition of diseases like scabies.
- According to the fourth World Health Organization (WHO) report on NTDs released on April 19, 2017 India has achieved the target for the elimination of visceral leishmaniasis (kala azar), in 82% sub-districts.

4. Future prospectus

The neglected parasitic infections are common conditions in the world. It affects at the poor people those who struggle to meet their daily basic needs and access basic health care services. However, these diseases typically go undiagnosed because of poor awareness among health care providers as well as the relative inaccessibility or unavailability of the diagnostic tests. Confirmatory diagnosis of these parasitic infections requires well established lab, reagents, advance diagnostic methods. Therefore, there is an urgent need to develop improved diagnostic methods. There is minimal surveillance data available and lack of disease burden information it hinder efforts to assess disease burdens, identify at-risk populations, and modes of transmissions. Finally, we need programs of health education to promote awareness for the neglected parasitic infections and to shape policies for control and prevention.

5. Control strategies

It is based on implementation of the five interventions recommended by WHO to overcome NTDs, namely: preventive chemotherapy, innovative and intensified disease management, vector ecology and management, veterinary public health services, and the provision of safe water, sanitation and hygiene^[13].

5.1. Preventive chemotherapy

it includes implementation mass drug administration (MDA). Several Pharmaceutical companies committed to donating drugs required for treatment including Sanofi Aventis donate Eflornithine and Melasoprol for Sleeping sickness, Novartis donate Triclabendazole for Fascioliasis, Johnson & Johanson donate Mebendazole for intestinal worms, Merck KgaA donate Praziquantal for Scistosomiasis and Gilead Sciences donates Liposomal amphoterecin B upto 2021 against Visceral Leishmaniasis^[50].

5.2. Intensified case management

It includes comprehensive training for health workers and village volunteers, as well as community level control programme such as surveillance, detection and case finding. Online courses are also available on Regional VCPH-<https://courses.campusvirtualsp.org/> for the surveillance, control and elimination of neglected diseases such as Visceral and Cutaneous Leishmaniasis, Schistosomiasis and Geohelminthiasis.

5.3. Vector control

WHO launched Global vector control response strategy for 2017-2030 it provides strategic guidance to countries and development partners for vector control as fundamental approach to preventing transmission of parasitic disease. It based on principle of integrated pest management including judicious use of pesticides.

5.4. Provision of safe water, sanitation and hygiene (WASH)

In August 2015, WHO launched a global strategy and action plan to integrate WASH aims to intensify the control and elimination of Neglected diseases^[51, 52, 53].

6. Conclusion

These NPI's are acquired in their own immediate environment where substandard housing, lack of access to safe water and sanitation, chronic hunger, filthy environments, close contact vectors, domestic animals and livestock contribute to their efficient transmission. The NPI's are may be due to poor population with low visibility and little political voice; and also may be due to the underreporting and missed diagnoses, because of lack of awareness of clinician and poor availability of optimal diagnostic facilities. According to recent reports, there is salient achievements control of neglected diseases due to implementation of the five control strategies recommended by WHO to overcome NPI's are preventive chemotherapy by mass drug administration, innovative and intensified disease management, integrated vector management that combine bed net with insecticides are key elements for control of vector born parasitic infection, veterinary public health services and the access of safe water, maintenance of sanitation and hygiene. No single strategy can control the neglected parasitic diseases; it needs integration of all control strategies simultaneously. Still we have to work on optimal diagnosis tests, vaccination and integrated vector management and improve surveillance and disease burden assessments together as part of overall efforts to strengthen health system.

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