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Distinct blue print to restraint neglected tropical diseases

Bhagwati K. Gauni Mehariya[1]***, Krunal R. Mehariya** [1, 2]

[1]National Facility for Drug Discovery Complex, Department of Chemistry, Saurashtra University, Rajkot - 360 005, Gujarat, India.

[2]Department of Chemistry, Gujarat Science College, Ahmedabad, Gujarat, India.

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Abstract: Since few decades many developing countries are bearing the strain of Neglected Tropical Diseases (NTDs) and they are the most common infections of the World's poorest people living in Africa, Asia and Americas. Till date, neglected tropical diseases imitate a group of conditions whose cluster level is obtained from deficiency of efforts directed to their declination. Global efforts have been done to control thirteen parasitic and bacterial infections that affect more than 1.4 billion people. The global usage of drug therapies for reducing the severity of NTDs was introduced few years ago. This singular approach should be elaborate to more extensive set of tools like coordinated community-based programs, vector control, local training, education and environmental change. In more, accelerated schedule is crucially needed to establish adequate diagnostic, preventive and therapeutic interventions to stay one step ahead of the evolutionary adaptation system of disease-causing microorganisms and parasites [1] [2].

Key words: Neglected Tropical Diseases; Parasite; Microorganisms; Drug Therapy.

Introduction

Neglected tropical diseases (NTDs) characterize a set of conditions whose group label is resultant from the lack of efforts directed to their eradication [1]. The world's poorest people living in Africa, Asia and the Americas most commonly get infected by the Neglected Tropical Diseases (NTDs) [4]. Leading to the socio-economic encumber in the poorest regions of the world, Neglected tropical diseases cause intense suffering and death. There is an extensive need for the adqaueate treatment, vaccination and analysis for such diseases. There is a significant scarcity of transformation from early stage scientific research into actual products for patients and impossible obstructions for some products and technologies to become inexpensive for the poor people most affected by these diseases. Although there are some access to the solutions that exist but the affordability to those solutions is not easy for the poor patients who get affected by these types of diseases. Scrutinisation of this problem has been more populated through the Research and Development (R&D) pipeline in the last few years. If in some places there is any availability for the real products then also control and elimination of NTDs is limited due to two main reasons: (1) failure of the market to imply the right strategy to put the real products that can be easily available to the poor patients and (2) public policy failure to correct this obstinate "if there is no money-there is no cure" [3].

The reasons for the inhibiting the socio-economic progress throughout the developing countries are ancient and entrenched infectious diseases that permanently vanish human potential in a large potential.

Deprived water supply, inadequate housing and sanitation, poor nutrition, low literacy rates, rudimentary health systems, constant presence of insects and other disease vectors in the house hold are the favorable conditions for NTDs in poor countries. Every year NTDs impair the lives of many people often with unfavorable effects starting in early life itself.

The neglected tropical diseases (NTDs) mostly affect the world's poorest people living in Africa, Asia, and the Americas [4]. The pattern of prevalence and disease load is differing according to geographic and regional occurrence. Such criteria for the NTDs in China and East Asia [5], the Americas [6-8] and Sub-Saharan Africa [9], correspondingly were reviewed in previous years. Here we review existing knowledge on the incidence, distribution and disease load of the NTDs in South-East Asia focusing on aspects meticulous to the region.

***Corresponding Author:**
Bhagwati K. Gauni Mehariya,
Centre of Excellence (CoE),
National Facility for Drug Discovery Complex,
Department of Chemistry,
Saurashtra University, Rajkot - 360 005, Gujarat, India.
E-mail: b.gauni@gmail.com, krunal.mehariya@gmail.com

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Table 1: The Major NTDs in India and South Asia Ranked by Prevalence.

Disease	Number of Cases in India (Percentage of Global Disease Burden)	Number of Cases in India and South Asia (Percentage of Global Disease Burden)	Reference
Ascariasis	140 million (17%)	237 million (29%)a	[12,13]
Trichuriasis	73 million (12%)	147 million (24%)a	[12,13]
Hookworm infection	71 million (12%)	130 million (23%)a	[12,13]
Lymphatic Filariasis	6 million (5%) (based on 0.53% prevalence)	<60 million (50%)b	[14]
Trachoma	1 million (1%–2%)	2 million (2%–4%)a	[15, 16]
Visceral Leishmaniasis	Not determined	200,000–300,000 cases (40%–60%)	[17,18]
Leprosy	87,190 registered cases (41%)	120,456 registered cases (57%)b	[19]
Rabies	20,000 cases/deaths (36%)	≥20,000 cases/deaths (36%)	[11,20]
Japanese encephalitis	1,500–4,000 (incidence)	1,000–3,000 (incidence, Nepal); 100–200 (incidence, Sri Lanka)	[21,22]

Neglected Bacterial infections

Leprosy

Being one of the oldest disease known to mankind, leprosy affects skin and peripheral nerves which can lead to crippling deformities of the hands, feet and face if it is left undiagnosed or untreated. The causative agent of the leprosy is *Mycobacterium leprae*. The poor and other vulnerable and marginised groups of populations are the victims of leprosy that are exposed to prejudice, discrimination, stigma and ostracism [10]. Since the early 1980s, WHO promoted a combination of three drugs that leaded to implementation of multi-drug therapy (MDT). Due to MDT there has been a dramatic decrease in global leprosy cases i.e. from 1.2 million cases in 1985 to 0.25 million in 2009 [10]. Due to success of MDT, the WHO passed a resolution to work towards the elimination of leprosy as a public health problem, defined as a prevalence of, 1 case per 10,000 population [11]. There were 122 leprosy-endemic countries with a national prevalence of 0.1/10,000 population in 1985. By 2010, 121 of the 122 countries have achieved the leprosy elimination goal at the national level and many of them have also achieved the goal at the sub-national level too. The worldwide leprosy program has been one of the potent success stories in public health.

Some of the key factors which attributed to the successful eradication of leprosy in South-East Asian regions are : 1) 1) strong political commitment and allocation of resources by national governments; 2) a free supply of anti-leprosy drugs from WHO, thanks to the generous grants from the Nippon Foundation and the Novartis Trust for Sustainable Development; 3) the leadership provided by WHO and effective coordination with national programs and partners; and 4) strong partnerships involving the World Bank, other United Nations (UN) agencies, international/national nongovernmental organizations, and support of key groups like media, religious leaders, local community leaders, and youth/women's groups. Currently, of the world's 212,000 registered cases of leprosy, more than one half still occur in South Asia [11].

The key factors which contributed to the success of elimination of leprosy are: 1) Provision of resources by national governments and strong political commitment. 2) free supply of anti leprosy drugs by WHO grants. 3) Effective leadership provided by WHO and coordination with national programs and partners. 4) Strong partnerships involving the World Bank, other United Nations (UN) agencies, international /national nongovernmental organizations, and support of key groups like media, religious leaders, local community leaders, and youth/women's groups [11]. Making strong integration of leprosy services into general health system through capacity building and skill development, in order to ensure and sustain quality leprosy services, including diagnosis and treatment at all levels. This criterion has been proven the key factor for gains in India's leprosy elimination efforts [23].

An expert group meeting organized by the Novartis Foundation in January 2014 at Zurich, Switzerland, concluded that chemoprophylaxis with single-dose rifampicin (SDR) was efficacious in reducing the risk of developing leprosy, although the protective effect appeared to be smaller in close contacts than distant contacts16. Therefore, blanket approach may be more appropriate in endemic areas. Further research is needed to determine the effect of chemoprophylaxis with repeat doses of rifampicin, other regimens (*e.g.* Rifapentine or ROM), or in combination with BCG immune prophylaxis. Also the duration of long prophylactic treatment and the specific biomarkers that can differentiate infected (asymptomatic) contacts from non-infected contacts need to be evaluated [24].

Leptospirosis

Although Leptospirosis is believed to be one of the significant NTDs in South Asia, there is no effective prevalence and disease burden information. However, because of its association with flooding, Leptospirosis is believed to be an important cause of acute febrile illness in children and aseptic meningitis, especially in the monsoon and immediate post-monsoon seasons [27]. The disease is endemic in the Indian states of Kerala

(where the sero prevalence is especially high among high-risk groups such as sewage workers, hospital sanitary workers, and fisherman), Tamil Nadu, and the Andaman and outbreaks are common in the slums of Mumbai [28].

Active Trachoma

Throughout the World trachoma is a leading cause of visual impairment and blindness. According to the WHO's world trachoma atlas using data from 2003, approximately 1 million cases of trachoma occur in India, particularly in Rajasthan [15], and 200,000–300,000 cases in Afghanistan, Nepal, and Pakistan [19]. These cases represent less than 5% of the world's trachoma disease burden [26]. However, other sources indicate that India may account for a much larger contribution to the global trachoma disease burden [11,15].

Neglected Viral infections

Chikungunya

Being first identified in Tanzania in the early 1950s it has been caused many periodic outbreaks in Asia and Africa since the 1950s. In Chikungunya significant pain occurs in the joints and the pain can stay for several weeks. Many times it can be misdiagnosed with Dengue because it shares some clinical signs in areas where dengue is common. Between 2001 to 2007 many countries reported Chikungunya outbreak. In India there was an outbreak of Chikungunya in 2006 in which 1.4 million cases were reported with the causative agent of *Aedes aegypti* that was implicated as the vector [29].

Rabies

In south Asia Rabies has been proven an important neglected tropical disease. Canine rabies is enzootic in India and it is estimated that India accounts for 36% of the world's deaths from rabies (approximately 20,000 or more), with between 30% and 60% occurring in children, and most of the cases in rural areas [30]. All these deaths are preventable through prompt medical attention comprised of wound cleaning and care along with post-exposure prophylaxis with rabies vaccine. Canine population of India is estimated as high as 25 million [30]. This scenario makes a national program of canine mass vaccination difficult even though it is considered one of the most cost-effective ways to reduce rabies deaths [31]. Indian pilot project to prevent human rabies deaths was launched by National Centre for Disease Control in 2008 in five Indian cities. This program was consisting of programs to increase awareness by the public and health care professionals about the importance of immediate medical attention to animal bites and scratches [30]. In addition, Nepal is making its own rabies vaccines for human and dogs while Sri Lanka has made great strides in eliminating dog rabies [32]. In all enzootic countries it was recommended that comprehensive national rabies control programs should be established [31].

Japanese Encephalitis (JE)

It is believed that JE has been introduced from East Asia to South Asia within the last half of the 20th century [33]. Due to its recent emergence in the region, JE affects both children and adults in Northern India, Nepal, Sri Lanka, whereas it is predominantly a pediatric disease in the Asia-Pacific region [33]. Due to lack of vaccination programs and possible other interventions, the incidence of JE in Bangladesh, India, and possibly Pakistan was noted previously to be on the rise, whereas it had decreased in Nepal and Sri Lanka, where both surveillance and vaccination programs are in place [34]. Currently India, Bangladesh and Pakistan exhibit the highest JE disuse burden in South Asia [34]. The factors like population growth and irrigated rice farming creates suitable breeding sites for mosquito vectors has been proven key factors responsible for JE emergence in South Asia. The Indian Ministry of Health has recently developed plans for surveillance and national vaccination of children; immunization programs have begun in both Tamilnadu and Uttar Pradesh [34]. Around 9 million children were vaccinated in India in 2006, and since then vaccination programs have been introduces into all 62 endemic districts [35].

Dengue

The first epidemic of Dengue in India occurred in Kolkata and the Eastern coast in 1963-64 which subsequently reached the entire country with all four dengue serotypes [36]. Throughout the 19th and 20th centuries at least a dozen other epidemic dengue like illness were recorded. In 1987, dengue hemorrhagic fever was first reported in India with a large outbreak in Delhi in 1996. Initially only urban areas were affected but it has spreaded to rural areas with the occurrence throughout the year [36]. The first case of was appeared in the year of 2004 in Nepal and Bhutan [37]. Since 2006 the overall cases of dengue has increased in WHO's South East Asia regions [11].

Protozoan infections

Amoebiasis and Leishmaniasis represent the highest burden protozoan NTDs.

Amoebiasis

Amoebiasis is one of the important protozoan infections, especially in India and Bangladesh. There are minimal surveillance data available and no known disease burden information. Among the lack of information regarding the extent of this infection is the absence of effective widespread testing to differentiate amoebiasis caused by pathogenic *Entamoeba histolytica* versus the non-pathogenic *Entamoeba dispar* [38].

Visceral Leishmaniasis (VL)

Visceral Leishmaniasis is also known as Kala-Azar is estimated to affect 200,000-300,000 people in South Asia, representing more than 60 % of the World's cases of VL [17]. Many of the affected areas of South Asia's VL cases are contiguous areas of Bangladesh, India and Nepal [18]; in India it is mainly found in the state of Bihar, as well as in some neighboring districts in Uttar Pradesh, and in West Bengal [39]. In South Asia is caused by *Leishmania donovani* and transmitted to humans by the bite of an infected female sandfly, *phlebotomous argentipe*s. This disease lowers immunity, causes persistent fever, pancytopenia and enlargement of the spleen and liver, and leads to very high mortality untreated cases. An important complication is Post Kala-azar dermal leishmaniasis (PKDL). Chronic source for further transmission created by numerous parasites loadged in the lesions in the skin. VL is one of the important opportunistic infections of patients with HIV/AIDS [40]. Some important risk factors that excel the survival of the insect vector and foster disease transmission are mud walls, dumbness in houses, ad peri domestic vegetation [17]. Many times women often delay seeking VL treatments and more likely to die from their infection. In some cases the presence of cattle is associated with an increased risk of acquiring the infection [41]. This disease tends to cluster at the household level and entire villages can become infected during a VL epidemic within short time period [41]. WHO targeted the elimination of VL in South Asia [17], defined as an incidence of 1 case per 10,000 population at each endemic district. In 2000 the goal elimination was received when the health ministers of India, Bangladesh and Nepal met in Kathmandu, Nepal under the auspices of the WHO, by the joint action strategy for the goal of eliminating VL by 2015 by administrative commitment [18]. This task was necessary, based on the finding that 50 % of VL cases occur in the border districts of these three countries [18]. After the ministerial meeting, a draft strategic plan was developed and endorsed by the three countries during an inter-country meeting held in Varanasi, India, in November 2003. The reviewer authority for this plan was the Regional Technical Advisory Group (RTAG) for Kala Azar held in India, December 2004, and was finally adapted by the National governments and partners at a meeting in India, in August 2005. The major components of this strategy include: 1) rapid diagnosis wherever possible with rk-39 and prompt treatment with the oral drug miltefosine, injectable paromomycin, or liposomal amphotericin B [17, 18]; 2) vector management which includes bed nets and indoor residual spraying with DDT and other agents [17]; 3) effective disease surveillance; 4) clinical and operational research [18]; 5) social mobilization and partnership [18].

Helminth Infections

The most important helminth infections in South Asia consist of three soil transmitted helminth infections, i.e. ascariasis, trichuriasis and hookworm infections, lymphatic filariasis.

Soil-Transmitted Helminth Infections

Theses helminth infections represent the three most popular NTD in South Asia. Ascariasis (*Ascaris lumbricoides* infection) is the most common helminth infection and NTD in the region, with more than 200 million cases, followed by more than 100 million cases of trichuriasis (*Trichuris* trichuria) and hookworm, respectively [12,13]. *Necator americanus* accounts for most of the world's cases of human hookworm infections. In Uttar Pradesh and West Bengal States mined infections with both *N. amricanus* and *Ancylostoma duodenale* also occur as well as pure *A. duodenale* infections [42]. *A. duodenale* also cause infantile hookworm [43]. For Pakistan, waste water used in agriculture was found to be a important risk factor for hookworm infections [44]. India followed by Bangladesh accounts for approximately one-quarter of the world's cases of soil transmitted helminthiases [42]. Most recent data are available from the Global Atlas of Helminth Infections [45]. Because of their pronounced impact on child growth and development, in 2001 the 54th World Health Assembly established a target to reduce the prevalence and the intensity of soil-transmitted helminth infections in all countries by 50% and achieve a target of regular deworming of at least 75% of school-age children at risk [11].

Lymphatic Filariasis (LF)

Lymphatic Filariasis (LF) is the most undermined and disfiguring disease in South Asia and all of the cases are caused by *Wuchereria bancrofti* [14]. The mature worms inhabit the lymphatic systems that in last stages lead to lymphoedema and elephantiasis. The disease predominately affects poor and marginised groups [49]. Disabilities and deformities associated with LF result in heavy economic losses and loss of livelihood [50]. The WHO South East Asian region accounts for the single highest disease burden of LF, with approximately 50% of the estimated 120 million cases globally and 67% of disease burden when measured in disability-adjusted life years [14]. 40 % of the LF global disease burden is accounted by India alone [29]. Impaired worker productivity resulting from lymphoedema of the lower limbs and hydrocele leads to huge socioeconomic impact. India loses almost US$1 billion annually from LF, while in a recent qualitative study in Sri Lanka, Perera *et al.,* [50] have also articulated LF's social stigma. In South Asia, the nations of Bangladesh, India, Maldives, Nepal, and Sri Lanka are endemic for LF [50].

LF is targeted by WHO for elimination as a public health problem, defined as a microfilaraemia rate of 1%. In 1997, the World Health Assembly passed a resolution to work towards LF elimination, and in 2000 the WHO's Global Program to Eliminate LF established a goal to eliminate the infection by 2020 [14]. The main strategies are: 1) annual MDA with two drugs, DEC and albendazole, to the entire eligible population for 5–6 years, and 2) home-based disability alleviation and prevention [14]. To date, Sri Lanka has completed and stopped MDA, while India has implemented MDA with almost 100% geographical coverage of its endemic areas [14]. India's National Vector Borne Disease Program for LF elimination is impressive by its sheer scale and scope [28]. Today, with treatments offered to the entire endemic population of 600 million people, MDA for LF in India is that country's largest national public health intervention [14]. The overall prevalence of microfilaraemia for LF was cut in half between 2004 and 2008 and today the prevalence is 0.53% [14]. Bangladesh, Maldives, and Nepal are also implementing MDA with high rates of coverage [14].

Conclusion

Extensive programs to eliminate some of the highest prevalence NTDs are under way in South Asia. They consists activities of the Global Program to eliminate LF, which is conducting national programs of MDA, together with international VL elimination efforts emphasizing the large number of cases occurring in the border areas of Bangladesh, India and Nepal and national programs of MDT for Leprosy. Japanese Encephalitis has recently emerged in South Asia but it may also be controlled or eliminated through national programs of comprehensive vaccination. Other national control programs especially for Trachoma and soil transmitted helminth infections and efforts vaccinate against canine rabies needs to be expanded. These programs require integration with improvements in sanitation and access to clean water. Integrated vector management that promotes the bed nets with insecticides are key elements for the control of VL, CL, and the Arbovirus infections. Some new control tools are under development that can facilitate NTD and other disease elimination efforts are new or improved vaccines under development for cholera, dengue, hookworm infection, Leishmaniasis and malaria [48]. There is an vital need for better surveillance and disease burden assessments for most of the NTDs, but especially for amoebiasis, leptospirosis, and for linking MDA, vaccinations, integrated vector management, and improved surveillance together as part of overall efforts to strengthen health system in the region.

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