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Introductory Chapter: Neglected Tropical Waterborne Infectious Diseases - Strategies for Mitigation

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<http://dx.doi.org/10.5772/intechopen.74322>

1. Introduction

Uninterrupted rise in population growth and human development has exerted diverse pressure on the quality and quantity of water with privilege of access to them. The interface of the human health and water experiences the most immense pressure due to the emergence of water-associated pathogens. Water-associated infectious diseases are the principal cause of morbidity and mortality in the developing and underdeveloped countries. Interplay between pathogen and its environment is complex and crucial for understanding the survival of the species under selective conditions. Potential drivers for the emergence and reemergence of water-associated infectious diseases can be explained by environmental aberration, implementation of newer technologies, scientific advances and changes in human behavior and vulnerability [1]. Understanding the plausible cause of the emergence of water-associated pathogens has become the national and international priority areas, which is fundamental for drinking water treatment and water safety management [2]. Sanitation and hygiene are vital for human health, development and survival. Poor sanitation is coupled with huge range of diseases and approximately 2.4 billion people are underprivileged for advanced sanitation [3]. Many countries are able to provide adequate sanitation to their population, leaving people at risk for water, sanitation and hygiene (WASH)-related diseases. Fundamental source of emergence of water-associated infection is coupled with poor sanitation where contaminated fecal water resources are most predominant [4]. Waterborne infections are caused by either exposure to or ingestion of contaminated water and hence strongly coupled with scarcity, availability and access to water. Environmental factors, such as heavy rainfall, flooding, drought and temperature variation, may contribute for the emergence of water-associated pathogens [5]. Heavy rainfall and flooding are responsible for huge pathogen load in naturally existing

water resources. Certainly, heavy rainfall or flooding causes the overwhelming flow of sewage treatment plants, dissipated animal-generated manures and redistribution or remobilization of contaminated water sediments [6].

Various kind of microbial pathogens are emerging from water and can be classified into specific categories. The most significant ones are arises from fecal contaminated water sources with high number of viruses, bacteria and parasites [7]. Based on the origin of the etiological agents, water-associated infectious diseases have been well categorized into five disease groups. So far, the water-associated diseases have been the major priority area of national and international government agencies for access of quality water for drinking and other uses. However, some of the water-associated pathogens fall into the category of neglected tropical diseases (NTDs), which need further attention with improved management system [8]. This chapter focuses on the neglected tropical waterborne infectious diseases including strategies for mitigation, prevention and integrated control such as vaccine and drugs.

2. Classification of water-associated pathogens

Water-associated infectious diseases can be broadly classified as water-borne, water-based, water-dispersed, water-related and water-washed [9]. Water-borne diseases can be described as microorganisms emerged from consumption of fecal-contaminated water and can be divided into four subcategories, including enteroviruses, bacteria, protozoa and helminthes [10]. Enormous range of diseases are caused by water-borne infection where foremost diseases are typhoid fever, cholera, bacillary dysentery, gastroenteritis, leptospirosis, poliomyelitis, aseptic meningitis, infectious hepatitis, amoebic meningoencephalitis and ascariasis [11]. Unlike water-borne, water-based etiological agents are primarily worms that spend a part of their life cycle in water bodies. The best known classical example of water-based infectious disease is schistosomiasis [12] caused by a human contact with water infested with the larva of some parasitic worms known as cercariae. Water-dispersed incorporates infectious etiological agents which proliferate in water bodies and may enter into the human body through respiratory tract. The most prominent water-dispersed disease is Legionellosis (Pontiac fever) caused by *Legionella* results in pneumonia [13]. Water-related infectious diseases include vector-borne diseases where the vector inhabitants and the related intensity of the disease or outbreak depend on the presence of environmental water [14]. Burden of infection dynamics of water-related infectious diseases is linked with hydroclimatological drivers across a broad range of spatial and temporal scale. Water-washed diseases can be caused by poor personal and domestic hygiene due to clean water deprivation resulting in contact of eye or skin with contaminated water. A broad range of diseases can be assigned in this category including shigellosis, trachoma, leprosy, skin infections, ulcers, scabies and conjunctivitis [15]. Despite the well-categorized water-associated diseases, few of them have been grouped as neglected tropical waterborne infectious diseases, including trachoma, schistosomiasis, leptospirosis, human African trypanosomiasis, dengue, lymphatic filariasis and many others, which have been listed in **Table 1**.

Category	Diseases	Pathogens	Vaccine	Drugs
Water-washed	Trachoma	<i>Chlamydia trachomatis</i>	—	Trimethoprim-sulfonamide combinations, amoxicillin, macrolides, chloramphenicol and tetracycline
Water-based	Schistosomiasis	<i>Schistosoma</i>	Sh-28-GST, Sm-14, schistosome protein-calpain (Sm-p80)	Praziquantel
Waterborne	Leptospirosis	<i>Leptospira</i>	—	Cephalosporins, cefotaxime and ceftriaxone and penicillin G
Water-related	Lymphatic filariasis	<i>Wuchereria bancrofti</i>	—	Mectizan, diethylcarbamazine and albendazole
Water-based	Onchocerciasis	<i>Onchocerca volvulus</i>	—	Ivermectin
Water-related	Dengue	Dengue virus	Dengvaxia, DENVax, LATV Δ30	Suramin, lovastatin, pentosan polysulfate, castanospermine (CSP) and deoxynojirimycin
Water-related	African trypanosomiasis	<i>Trypanosoma brucei</i>	—	Pentamidine, suramin, melarsoprol, eflornithine, nifurtimox
Water-based	Dracunculiasis	Guinea worm	—	—

Table 1. Neglected tropical water-borne infectious diseases, category, available vaccine and drugs.

3. Epidemiology

A global database for water-associated pathogens and diseases has been established based on Global Infectious Diseases and Epidemiology Network (GIDEON). The infection dynamics and burden of water-associated infectious diseases can be linked to hydroclimatological drivers across a wide range of spatial and temporal regions [16]. Disease prevalence can be significantly correlated with the exposure and transmission rate, which are affected by environmental factors such as rainfall, air/water temperature and seasonal variability. For example, flood in an area may cause the contamination of drinking water sources with raw sewage and washing out of the etiological agents from open defecation sites [17]. In general, rainfall may affect human activities related to personal hygiene and water contacts potentially increasing the transmission risk. Drinking water and recreational settings are the most prominent source of water-associated infections.

The epidemiology of water-associated NTDs has been discussed here. A water-washed bacterium *Chlamydia trachomatis* causes trachoma. The bacterium is transmitted through personal contact and causes trichiasis if left untreated. The disease is mostly prevalent in areas with poorly developed water sanitation facility with almost 8 million people visually impaired and approximately 500 million people at the risk of infection [18]. Water-based NTD, schistosomi-

asis, caused by a human contact with water infested with the larva of parasitic worms known as *cercariae*. Approximately, 206.5 million people required treatment for schistosomiasis in year 2016 and around 700 million people are at risk [19]. So far, three schistosome species have been documented including *Schistosoma haematobium* known to cause urogenital infection and reported primarily in sub-Saharan Africa, *Schistosoma japonicum* known for intestinal infection and has been reported in Indonesia, Philippines and People's republic of China and *Schistosoma mansoni* which also infects intestine and has been reported in Brazil, Caribbean island and sub-Saharan Africa. A water-related, human African trypanosomiasis (HAT), commonly known as sleeping sickness, is caused by parasitic protozoa known as trypanosomes. The disease transmission is prevalent in sub-Saharan African countries where it is known to transmit through tsetse fly. From last 50 years, significant reduction in the number of new cases has been achieved in year 2009 where the number of reported cases was less than 10,000 [20]. Another imperative water-related NTD is dengue with an estimated 500,000 people with severe dengue necessity of hospitalization annually and approximately 2.5% of them die. According to WHO, around 128 countries are at risk for dengue infection with an estimated 3.9 billion people [21]. Leptospirosis is endemic in several countries of South-East Asia where most of the human infection reported from India, Sri Lanka, Indonesia and Thailand during the rainy season. So far, major outbreaks have been reported in Jakarta (2003), Mumbai (2005) and Sri Lanka (2008). Current available reports are suggesting that the global incidence rate is ranging from 0.1 to 10 in 100,000 annually [22]. Lymphatic filariasis caused by a parasite *Wuchereria bancrofti*, which is responsible for 90% of the cases. WHO launched Global Programme to Eliminate Lymphatic Filariasis (GPELF) in year 2000, and currently, 856 million people in 52 countries are living in areas which need preventive chemotherapy to reduce the transmission level [23].

4. Strategies for mitigation

The estimated 1 billion of the world's poorest population is affected by NTDs that comprise parasitic, bacterial and viral agents causing 534,000 deaths per year [24]. The NTDs are highly endemic in rural regions and in low-income countries with an average income less than US\$2 a day. This weaker section is unable to make any attempt in improving their children growth and development, education and malnourishment. As the target of NTDs is the poverty-stricken people, the market for drugs and vaccines are not well supported by the pharmaceutical industry, as well as the number of drugs available for treatment of NTDs is also limited and unchanged since the middle of the twentieth century. The preventive approaches suggested by WHO for controlling NTDs are case management, preventive chemotherapy, vector control, improved quality water and sanitation and zoonotic disease management [25].

The leading health organizations, such as WHO, CDC and UNICEF, have initiated various sustainable strategies across the globe to provide 2.3 billion unprivileged people access to basic sanitation, hygiene and clean water (**Figure 1**). International Water Association (IWA) and WHO has introduced Water Safety Plans (WSPs) that ensures the safety of water from its procurement to delivering to the consumers in urban and rural regions of 72 countries [26]. WASH is a global program strengthened with a vision to ensure safe drinking water and



Figure 1. Global schemes and strategies for implementation of WASH. The enforcement of global schemes and strategies such as Water Safety Plan, GLAAS and WHO-UNICEF JMP will provide sustainable management of WASH.

maintenance of sanitation and hygiene to unprivileged people. The implementation of WASH and prevention of NTDs are integrated [27]. Global Analysis and Assessment of Sanitation and Drinking-Water (GLAAS) was initiated by UN and WHO to monitor the implementation of WASH [28].

The systematic maintenance of WASH may prevent and control water-borne NTDs such as trachoma, dengue fever, dracunculiasis, lymphatic filariasis, schistosomiasis, soil-transmitted helminthes and onchocerciasis (river blindness). WHO commenced the Global Elimination of Trachoma by 2020 (GET 2020) with a vision to launch the SAFE strategy that links four components such as surgery, antibiotics, facial cleanliness and environmental improvements (SAFE) to tackle trachoma [29]. This infectious disease is accountable for 3% of world's blindness, where an estimated 8 million people are irreversibly visually impaired and another 84 million cases are in need of treatment [30]. Likewise, WHO and UNICEF jointly monitor a program called the comprehensive strategy for the control and prevention of worms such as soil-transmitted helminthes (STH)—intestinal worms such as ascariasis, hookworm and trichuriasis [31]. Children without worms (CWW) advocate about maintenance of water, sanitation, hygiene education, deworming (WASHED) in order to discontinue the cycle of STH reinfection [32]. The World Health Assembly (WHA) in May 2012 has urged to eliminate schistosomiasis by providing essential drugs, practicing safe WASH and focusing on health education [33]. Dracunculiasis (Guinea worm), another waterborne NTD, has been adopted by WHA with a goal to achieve complete absence of Guinea worm disease cases for 3 or more years. Later, Guinea Worm Eradication Program was lead in partnership with Centers for Disease Control and Prevention (CDC), UNICEF and the Carter Centre [34]. Lymphatic filariasis and onchocerciasis are also targeted in WHO 2020 for eradication of NTDs. The London declaration to combat NTDs has estimated that US\$785 million has been donated to NTD programs to strengthen and support drug availability and its distribution and research and development [35].

5. Prevention and integrated control

With the rising number of cases of water-associated infectious disease, there is an urgent need to regularly monitor the basic services of safe drinking water, sanitation and hygiene. The water resources are rivers, lakes and streams that replenish the groundwater table, and further, the water is stored in high-capacity storage tanks or else are directly delivered at the dwellings via piped or nonpiped facilities. The contamination of water resources due to open defecation near rivers, washing clothes, infiltration of solid wastes and chemicals from industries or bathing of animals like buffaloes deteriorates the quality of water. The contamination-free drinking water is the basic necessity for one and all without any inequality. The processing and pretreatment of the unsafe adulterated water from the source or because of the handling and storage issues could be used for drinking or in food preparation [36]. Numerous methods in combinations are used to minimize the microbial load of drinking water such as aeration, storage and sedimentation of water, filtration, disinfection of water and UV rays exposure. Various awareness programs regarding the basic hygiene facilities are necessary to be promoted to educate the population living especially in rural areas of developing countries. The global burden of mosquito-transmitted infectious diseases is rising at an alarming pace. The contaminated stagnant water kept in utensils for storage purpose is the dwelling of mosquito eggs and larvae. The mosquito-vector control program lists various methods such as avoiding water logging, repellents, insecticide-treated impregnated nets, larvivorous fish *Gambusia affinis*, and disinfecting their breeding habitats [37]. The use of toilets in every household and public place will end open defecation and prevent fecal contamination of water [38].

6. Vaccines and drugs

The prevention and treatment of pathogens using vaccines and drugs are the most robust and promising methods. Most of the vaccines for preventing waterborne infectious NTDs are undergoing clinical trial for human use; therefore, drugs are the only available option for their treatment. Vaccines in clinical trials for dengue are Dengvaxia, DENVax, LATV Δ30 [39], and for schistosomiasis are Sh-28-GST, Sm-14 and schistosome protein-calpain (Sm-p80) [40]. Pharmaceutical companies like Merck, Pfizer and GlaxoSmithKline have donated drugs to achieve the human health goals in targeting NTDs. Praziquantel is the readily available commercial drug for treating schistosomiasis, which is safe and effective to most of the people [41]. Other drugs available are albendazole, oxamniquine for *S. mansoni*, metrifonate for *S. haematobium* and artemether that kills worms in immature stage. The commonly used drugs for treating trachoma are trimethoprim-sulfonamide combinations, amoxicillin, macrolides, chloramphenicol and tetracycline, which are all effective against *Chlamydia trachomatis* [42]. The effective drugs for dengue are suramin, lovastatin, pentosan polysulfate, castanospermine (CSP) and deoxynojirimycin [43]. Dracunculiasis has no specific drug or a vaccine for its treatment and prevention [44]. Merck and WHO have collaborated for the development of ivermectin to combat against onchocerciasis (river blindness) and have certainly benefitted the African patients [45]. Merck, Eisai Co. Ltd. and GlaxoSmithKline had donated Mectizan, diethylcarbamazine and albendazole against lymphatic filariasis to the 300 million populations in endemic regions.

7. Conclusions and future perspectives

The water-borne infectious NTDs among the several other NTDs have majorly affected the poorest of the population, and with the support of health organizations and pharmaceutical industries, various steps are taken for the eradication of NTDs. To decrease the burden of NTDs, various preventive measures have to be strengthened for a sustainable solution such as maintenance of water, sanitation and hygiene in endemic areas, reducing disturbance of environment, provision of healthcare facilities to migrating populations to avoid exposure to NTDs, management of poverty in endemic area and regular risk assessment and surveillance of number of NTD cases. A decision-making body composed of scientists, microbiologists, clinicians and financial experts might be established in regions prone to water-associated infectious NTDs. The supply of water from the nearby source (stream/groundwater/piped/nonpiped) needs to be investigated to prevent the spreading of disease from few cases to endemics. The rapid point-of-care detection methods might be employed for the identification and quantification of the pathogens. With the identification of pathogen, diagnosis of severity of infection and its duration of exposure will determine the dose-dependent treatment. People sometimes choose self-medication over consulting a doctor, which might be risky as it increases the duration of illness. According to the type of water system and pathogens, proficient personnel might be required for their cleaning and removal.

Acknowledgements

The authors are grateful to the Vice Chancellor, King George's Medical University (KGMU), Lucknow, and Director, Centre for Cellular and Molecular Biology, Council of Scientific and Industrial Research (CSIR-CCMB), India, for the encouragement and support for this work. SK Saxena is also supported by CCRH, Government of India and US NIH grants: R37DA025576 and R01MH085259. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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