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## Review Article

## Emerging diseases in Bangladesh: Current microbiological research perspective



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## ABSTRACT

Bangladesh has experienced a variety of diseases caused by natural dissemination of an array of pathogenic microorganisms into the environment. While cures for these diseases largely depend on the medication strategies of physicians, determining the reasons for disease persistence as well for the onset of reinfection is also essential. Routine diagnosis of common diseases usually means treatment with a range of appropriate medicines; however, failure of these medications because of the drug resistance of microorganisms accompanied by a lack of alertness about the etiology of diseases often leads to fatal results. The present review reports on emerging diseases in Bangladesh and focuses on associated microbiological research into ongoing diseases including enteric, urinary tract, and malarial complications. The viruses associated with acquired immunodeficiency syndrome and hepatitis are also discussed. Copyright © 2015, Buddhist Compassion Relief Tzu Chi Foundation. Published by Elsevier Taiwan LLC. All rights reserved.

## 1. Introduction

Infectious diseases are a pervasive menace worldwide. The incidence and prevalence as well as the emergence and re-emergence of a particular disease depend on the geographical and economic background [1–4]. Although most emerging diseases are conquered by new-generation chemotherapeutic agents, some complications remain uncontrolled and hence tend to spread rapidly as little is known about their etiology and subsequent management [1,2,5–9]. New and re-emerging infectious diseases such as severe acute respiratory syndrome, pneumonia, influenza, swine flu (H1N1), tuberculosis (TB), hepatitis, malaria, cholera, chikungunya, meningitis, Ebola virus diseases, food-borne gastroenteritis, salmonellosis, and campylobacteriosis continue to threaten global public health [2,5,10–24].

Major challenges in disease management have evolved as drug-resistant bacteria have emerged, posing a significant impact on the efficiency of chemotherapy [25]. During the past few years, the antibacterial activity of a number of drugs has decreased with the

concomitant onset of the drug-resistant pathogenic bacteria [6,25–27]. This has become one of the most severe public health issues worldwide, leading to fatalities from simple microbial infections followed by treatment-mediated complications from inactive drugs [25]. The worldwide increases in single drug-resistant bacteria, multidrug-resistant (MDR) bacteria, and extensively drug-resistant (XDR) bacteria are indeed well-known [26,28–37]. Incidences of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *S. aureus* (VRSA), coagulase-negative staphylococci, glycopeptides intermediate-sensitive *S. aureus*, vancomycin-resistant *Enterococcus* species, penicillin-resistant *Streptococcus pneumoniae*, extended-spectrum  $\beta$ -lactamase (ESBL)-producing bacteria, and carbapenem-resistant bacteria, especially in developing countries, have also been noted [6,26,38–45]. Bangladeshi people commonly consume large quantities of antibiotics not prescribed by physicians. Similar abuse of antibiotic agents also occurs frequently in India and Pakistan [25,46]. By contrast, in the United States and Europe, the levels of resistance of bacterial pathogens against antibiotics are lower because of stringency in prescription [46].

A variety of microorganisms triggering enteric diseases along with diseases such as cancer, respiratory and pulmonary infections, influenza, heart diseases, malaria, TB, dengue, liver cirrhosis, urinary tract infections (UTIs), diabetes, chikungunya, and opportunistic infections pose major public health-related complications in

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Bangladesh with consequent high morbidity and mortality [2,8,28,30,32,47–60]. The high-density population, lack of awareness of personal hygiene, inadequate microbiological processing of food and pharmaceuticals, defective water-distribution systems saturated with sewage pipelines, and above all the ineffectiveness of antimicrobial agents have been known to account for the onset of these diseases [25,26,61–66]. Hospital-acquired infections and drug-resistant infecting pathogens complicate treatment outcomes [25,26,48].

For the past 10 years, scientists and academicians, together with their international collaborators, have made efforts to understand many of the pathogenic mechanisms of emerging and re-emerging infectious diseases, to discover novel diagnostic methods with appropriate antiviral, antibacterial, and antifungal compounds and to develop vaccines [2,67,68]. For more than four decades, the Centers for Disease Control and Prevention in Bangladesh has collaborated with the International Centre for Diarrheal Disease Research, Bangladesh to mitigate health-related problems and strengthen the country's capacity to diagnose and detect emerging infectious diseases [47]. In addition, microbiological experiments are being conducted to identify etiologic agents and find accurate remedies [8,28,30,32,49,52,53,58–60].

## 2. Microbiological studies of emerging diseases in Bangladesh

*In vitro* microbiological studies of different diseases in Bangladesh have revealed the growth and proliferation of a large number of bacterial pathogens. Microbiological studies have mostly been carried out using conventional differential and selective culture media, morphological tests, confirmative biochemical identification, antibiogram assays, and tests for ESBL and carbapenemase production as described earlier [69–73]. In most cases, a huge bacterial onset with an alarming threat of MDR would suggest the appropriate bactericidal action together with the effective therapeutic events.

### 2.1. Microorganisms associated with enteric diseases

Commencement of enteric diseases (e.g., cholera, diarrhea, dysentery) in the developing countries principally occurs because of microbiologically contaminated food and water associated with an unhygienic lifestyle [61–63]. The global cholera burden has been estimated to be 3–5 million cases and accounts for a total of 100,000–130,000 deaths annually [74]. Bangladesh is at a very high risk of cholera [61,75,76]. A study conducted by Acharjee et al [61] quantified significant *Vibrio* spp. in meat, fish, vegetables, fruits, street food, bakery shop foods, fast food, sweets, and dairy products. Their drug-resistant traits pose a serious public health hazard. Hossain et al [55] estimated that the prevalences of bacteria other than *Vibrio cholerae* causing diarrhea in children were 2% for *Yersinia* spp., *Aeromonas* spp., and *Plesiomonas* spp., 6% for *Vibrio* spp., 10% for *Salmonella* spp. and *Shigella* spp., and 14% for *Campylobacter* spp.

### 2.2. Opportunistic pathogens and intestinal parasites associated with human immunodeficiency virus

The interactions between human immunodeficiency virus (HIV) and opportunistic pathogenic bacteria and other intestinal parasites are well-known, and they influence the health status of people with HIV/acquired immunodeficiency syndrome. Noor et al [8] conducted a study to detect enteric parasites in HIV-infected patients with enteric diseases. Intestinal parasitic pathogens were found in around 77% of patients with HIV, which were also associated with the growth and proliferation of opportunistic

pathogens. These included *Cryptosporidium* spp., *Blastocystis hominis*, *Entamoeba histolytica*, *Hymenolepis nana*, *Isospora belli*, *Giardia lamblia*, *Cyclospora* species, *Ascaris lumbricoides*, and *Trichuris trichiura*. *Cryptosporidium* spp. were found to be prominent in HIV-positive patients suffering from diarrhea, and polyparasitic infections were demonstrated in chronic cases with low CD4 counts. Noor et al [49] noted that common opportunistic infections associated with HIV included diarrhea, pulmonary TB, gland TB, skin lesions, and fever. Other problems associated with HIV mainly include respiratory and gastrointestinal tract complications, bronchitis, UTIs, sexually transmitted diseases, weight loss, pharyngitis, prostatitis, skin rashes, and oral ulcerations. However, the HIV prevalence rate in Bangladesh is still estimated to be very low [8,49].

### 2.3. Microorganisms associated with burn wounds

A major fraction of burn wound samples was found to harbor total aerobic viable bacteria up to  $10^7$  colony-forming units/mL. The predominant pathogens were *Pseudomonas* spp., *S. aureus*, and *Klebsiella* spp. followed by *Enterobacter* spp. and *Escherichia coli*. Most of the pathogens were found to be drug resistant and several isolates were noted to be MDR [26].

### 2.4. Drug-resistant TB in Bangladesh

TB, principally caused by *Mycobacterium tuberculosis*, is a major health problem globally [28,74,77–80]. In Bangladesh, there are > 350,000 new cases with 70,000 deaths annually [30,32,57,60]. Cases of MDR and XDR TB in Bangladesh are of extreme significance in overall public health management [28,32,81]. In addition to TB, MDR bacteria can result in various clinical complications followed by treatment failure when employing antibiotics [25,62,65]. A clinical investigation in Bangladesh revealed that > 70% of infecting bacteria were resistant to at least one of the commonly used antibiotics [25]. MDR bacteria including MRSA, methicillin-resistant *Staphylococcus epidermidis*, VRSA, methicillin-resistant coagulase-negative staphylococci, and penicillin-resistant *S. pneumoniae* are widely known to be difficult to eradicate [6,7,25,26,31,37,45,46,71].

### 2.5. Hepatitis B virus infection

Hepatitis B, an infectious illness caused by hepatitis B virus (HBV) is responsible for chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma, ultimately causing death [50]. Approximately 2 billion people have been reported to be infected with the HBV worldwide [50,54,58]. In Bangladesh, HBV infections can occur because of a lack of health education and vaccination [54]. Studies of HBV include the following: (1) detection of biochemical and serological markers of HBV infection other than HBsAg, (2) uncovering common risk factors associated with HBsAg positivity among patients suspected to have HBV infection, and (3) investigating the efficacy of vaccines for hepatitis B to reveal the immunological memory against the vaccine [50,54,58]. Detecting the serum HBV DNA level has proven to be comparatively effective in assessing liver disease activity [50,54].

### 2.6. Carbapenemase-producing *Klebsiella pneumoniae* and microorganisms associated with UTI

The resistance of *Klebsiella pneumoniae* against carbapenem is another rising global health issue [82,83]. Hayder et al [7] studied carbapenemase-producing *K. pneumoniae* in Dhaka, Bangladesh. A total of 647 *K. pneumoniae* isolates were found in 2800 patients with UTIs, bacteremia, wound infections, and respiratory diseases.

Thirty-one carbapenem-resistant isolates were found to harbor *K. pneumoniae* carbapenemase. An additional 287 isolates were ESBL positive [7]. Indeed, *K. pneumoniae* are the most predominant genera carrying ESBLs and are usually highly resistant to aminoglycosides, fluoroquinolones, and sulfonamides [84]. Carbapenemase-producing *E. coli* strains are also well-known [85,86]. From 2007 to 2011, 22 *E. coli* strains producing *K. pneumoniae* carbapenemase were isolated in Hangzhou, China. Twelve of these were isolated in 2011, suggesting an escalation in carbapenem-resistant *E. coli* in China [85]. A recent study conducted by Peirano et al [86] showed that 407 of 47,843 *E. coli* isolates had  $\beta$ -lactamase genes and 116 of the 407 isolates were positive for an array of carbapenemases.

UTI is a common clinical complication worldwide [87,88] with a high incidence in Bangladesh [6]. A study conducted by Noor et al [51] revealed that among 462 urine samples collected from patients with UTI, 100 were found to be culture positive. *E. coli* was the predominant organism, whereas *Klebsiella* and *Enterococcus* were also prevalent. Other bacteria isolated included *Pseudomonas* spp. and *Proteus* spp. An interesting aspect of ESBL production was noted in a study of UTI patients by Khan et al [6]. ESBL-producing microorganisms are known to exhibit important therapeutic complications as they develop resistance against third-generation antibiotics. In a previous study, *E. coli* was found to show stronger resistance against several antibiotics than isolates tested in Europe [89].

### 2.7. Microorganisms associated with malaria

Malaria is another prevailing public health issue in Bangladesh. The major microorganisms associated with malarial disease are *Plasmodium falciparum* and *Plasmodium vivax*. The former causes around 90% of malaria in Bangladesh [59]. The global impact of malaria has drawn interest in developing an effective diagnosis, especially in resource-poor settings. Jahan et al [59] conducted experiments on rapid diagnostic tests for malaria and endorsed the *OnSite* test based on antigen detection over the SD Bioline anti-Pf/Pv test based on antibody detection. However, both methods can detect multiple infections (caused by different species of *Plasmodium*) with a higher sensitivity and specificity than conventional microscopy. Therefore, these methods are expected to aid in the National Malaria Control Program.

### 3. Addressing the problem of emerging diseases in Bangladesh: Recommendations

In Bangladesh, the majority of people maintain a poor quality of life and have a meager education. Knowledge about the generation and subsequent spread of diseases is very scanty [2]. The first step to minimize emerging infections is to increase public awareness of hygiene. Knowledge about unhygienic handling of water and food is of significance [61,62]. Appropriate therapy with physician's recommendations can minimize treatment complications [6,25]. These actions could be regulated by governmental bodies employing health professionals. Another important clinical aspect is the study of neglected tropical diseases (NTDs), which are known to cover a wide range of infections predominantly affecting the poorest and most vulnerable individuals. In Bangladesh, these include lymphatic filariasis, trachoma, soil-transmitted helminths, leprosy, guinea worms, and visceral leishmaniasis [90].

### 4. Conclusion

Currently in Bangladesh, both governmental and nongovernmental organizations are working to eradicate health-associated

problems in the community. However, more emphasis should be given to conducting field and laboratory research on diseases of public health importance. Attention should be drawn to emerging diseases, such as respiratory complications, zoonotic diseases, vector-borne diseases, and NTDs, as well as other identified public health priorities. The research outcomes should be evaluated to enhance the overall management of disease prevention and control programs. Training and capacity building programs for health improvement are also important to minimize emerging diseases. Emphasis should be given to sharing of expertise and research findings with other nations as well as academic and research organizations. Finally, to successfully combat disease-causing microbial flora, pioneering microbiological research on the principal mechanisms underlying microbial pathogenesis both at the initiating stage and during disease progression is essential.

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