

Epidemiology of melioidosis in Bangladesh

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The pioneering work of Indian bacteriologist, C.S. Krishnaswami, and British pathologist, Alfred Whitmore, first identified the organism *Burkholderiapseudomallei*, among Burmese morphine addicts in 1911. Since then, it took a century to determine its source in the environment of the Indian sub-continent. The organism was recovered for the first time in 2011 from the soil of Gazipur District of Bangladesh.

However, the first case of melioidosis from Bangladesh was reported in 1964 in a 29 year old British sailor who was travelling through Bangladesh and stayed in Chittagong for 3 months. Since then, melioidosis has been sporadically detected in Bangladesh over last several decades. The first melioidosis case in a native Bangladeshi child was diagnosed in 1988. Subsequently, five more cases were detected in U.K among Bangladeshi immigrants from the Sylhet region from 1991 to 1999. Later on, at least 35 culture-confirmed melioidosis cases were detected among the diabetic patients in Bangladesh and all of these cases were diagnosed at Ibrahim Medical College and BIRDEM Hospital in Dhaka from 2001 to 2016.

So, it is evident that melioidosis is prevalent in Bangladesh. In order to determine the magnitude of exposure, two sero-epidemiological studies were conducted to elucidate the extent of melioidosis in the Bangladeshi population. In 2012, a hospital based serological survey using the indirect haemagglutination assay reported a 28.9% sero-positive rate among patients attending several tertiary care hospitals for unrelated ailments. The other study, conducted in 2013, used sonicated whole-cell antigen to determine anti *B. pseudomallei* IgG antibody by ELISA and detected a sero-positivity rate of 21.48% among healthy people attending the rural health care facilities of four northeastern districts of Bangladesh.

Analysis of the geographical distribution of melioidosis cases indicates that the disease is potentially endemic in eleven districts of the country. Out of these districts seven are located in the north and northeast region while the remaining four districts are located in the southern part of Bangladesh. As the majority of the cases were from northeastern districts of the country (like, Mymensingh, Gazipur, Sylhet and Dhaka) we consider those districts as the major endemic areas for melioidosis in Bangladesh. The disease is found to be highly seasonal with the majority of cases presenting during the rainy season (April to August), presumably because during this period the chance of exposure to the organism is highest.

The clinical presentation of melioidosis among Bangladeshi patients ranges from localized to systemic infection. However, no single clinical feature was found to be typical of melioidosis, though fever was present in 100% of cases. The most frequent presenting features include acute fulminant septicemia to a chronic debilitating localized infection characterized by abscess formation in different organs of the body. Although more than 50% cases presented with focal

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abscesses, non-suppurative infection such as septicemia, arthritis, UTI and pneumonia were also prevalent. In Bangladesh diabetes has been documented as the most commonly associated concomitant risk factor found in >95% of cases of melioidosis. Out of 35 melioidosis cases admitted at BIRDEM hospital, 6 (18%) patients died. Most of these cases presented with septicemia and died within 24-48 hours of hospital admission and before the diagnosis of melioidosis was made. This stresses the need for early diagnosis and initiation of appropriate treatment.

Phylogenetic analysis of 22 clinical and 2 environmental isolates of *B. pseudomallei* by multi locus sequence typing (MLST) revealed thirteen different sequence types (STs), of which 4 STs (ST- 1352, 1124, 761 and 756) were novel types. All the strains containing ST 56 were isolated from patients with septicemia. ST 56, present in 5 clinical isolates, was the most common variant present in Bangladesh, followed by ST 1007 (4 cases) and ST 1005 found in 2 clinical and 2 soil isolates. Presence of ST 1005 in the soil of Gazipur district as well as its presence in melioidosis patients from the same area indicated soil as the source and reservoir. Gene cluster analysis targeting Yersinia-like fimbrial (YLF) and *B. thailandensis*-like flagellum and chemotaxis (BTFC) gene demonstrated that all 24 isolates contained YLF gene cluster. None of the isolates was positive for BTFC gene cluster. YLF is found predominantly in the South Asian region. Apart from the four novel STs described above, all other STs that have been detected in Bangladesh are also present in Thailand, Cambodia, China and Vietnam and other neighboring countries. It is likely that human and/or animal trafficking between these areas played a major role in the dissemination of *B. pseudomallei*. However, further analysis with a wider range of isolates from these regions is required to confirm the source and distribution of the organism in the region.