

Study warns Diphtheria could become a major global threat

New Delhi, March 09 (India Science Wire): In a new health scare, a team of researchers from India, the UK and Russia, has found that Diphtheria, which is a relatively easily-preventable infection, has started to become resistant to several classes of antibiotics, and in future, it may even become immune to vaccination.

In a report, the team has also suggested that there was a possibility of the disease once more becoming a major threat across the globe because of the impact of COVID-19 on vaccination schedules in different parts of the world, coupled with a rise in the number of infections.

Diphtheria is a highly contagious infection. It can affect the nose and throat, and sometimes the skin. If left untreated it can prove fatal. In high-income countries, all babies are vaccinated against the infection. However, in low- and middle-income countries, the disease can still cause sporadic infections or outbreaks in unvaccinated and partially-vaccinated communities.

The number of diphtheria cases reported globally has been increasing gradually. In 2018, there were 16,651 reported cases, more than double the yearly average for 1996-2017 (8,105 cases).

Diphtheria is primarily caused by the bacterium *Corynebacterium diphtheriae* and is mainly spread by coughs and sneezes, or through close contact with someone infected. In most cases, the bacteria cause acute infections, driven by the diphtheria toxin - the key target of the vaccine. However, non-toxigenic *C. diphtheriae* can also cause disease, often in the form of systemic infections.

The researchers used genomics to map the infections, including a subset from India, where over half of the globally reported cases occurred in 2018. By analysing the genomes of 61 bacteria isolated from patients and combining these with 441 publicly available genomes that had been collected from across the world over 122 years (1896-2018), they build a phylogenetic tree - a genetic 'family tree' - to see how the infections are related, understand how they spread and assess the presence of antimicrobial resistance (AMR) genes and determine toxin variation.

The main disease-causing component of *C. diphtheriae* is the diphtheria toxin, which is encoded by the 'tox' gene. It is this component that is targeted by vaccines. In total, the researchers found 18 different variants of the 'tox' gene, of which several had the potential to change the structure of the toxin.

Diphtheria infections can usually be treated with several classes of antibiotics. While *C. diphtheriae*'s resistance to antibiotics have been reported, the extent of such resistance remains largely unknown.

The team looked for genes that might confer some degree of resistance to antimicrobials and they found that the average number of antimicrobial resistance genes per genome was increasing each decade. Genomes of bacteria isolated from infections from the most recent decade (2010-19) showed the highest average number of AMR genes per genome, almost four times as many on average than in the next highest decade, which was the 1990s.

In a report on their study published in Nature Communication today, the team said, “While our data does not, at present, highlight any efficacy concern in the currently used tox variant type 16 based diphtheria toxoid vaccine, the continually increasing toxin diversity and prevalence of non-toxigenic strains do however forecast a real possibility of vaccine escape and antitoxin treatment failure in future. While the current vaccine against diphtheria continues to remain largely effective, it is vital to conduct further in vitro and in vivo studies”.

The researchers were drawn from the Department of Biotechnology’s Translational Health Science and Technology Institute, Faridabad, Maharishi Valmiki Infectious Diseases Hospital, Delhi, Christian Medical College, Vellore, Tamil Nadu, World Health Organization, New Delhi, Ministry of Health and Family Welfare, New Delhi, Cambridge Institute of Therapeutic Immunology & Infectious Disease, University of Cambridge, Liverpool School of Tropical Medicine, UK, Gabrichevsky Research Institute for Epidemiology and Microbiology, Moscow, Russia, Northumbria University, Newcastle upon Tyne, UK.

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