Source : www.thehindu.com Date : 2021-04-04

RESEARCHERS FORESEE TRENDS IN DIPHTHERIA INCIDENCE

Relevant for: Science & Technology | Topic: Biotechnology, Genetics & Health related developments

Typical signs: Formation of white-grey pseudomembrane over parts of the throat, voice box and tonsils and swollen bull neck are considered stereotypical. | Photo Credit: Special arrangement

Researchers from India, the U.K. and Russia have analysed a large collection of 502 genomes sourced from over 16 countries and collected from over a period of 122 years of the bacterium that causes diphtheria – *Corynebacterium diphtheriae*. The results of this massive and collaborative study hint that we need to anticipate increase in incidence of diphtheria which may be fomented by the diversity of the species, emergence of variant toxin genes and progression of antimicrobial resistance.

They recommend that more *in vivo* and *in vitro* studies be undertaken to verify these hypotheses. The work was published recently in *Nature Communications.*

Diphtheria usually begins with angina (a type of chest pain) and tonsilitis symptoms, sore throat and mild fever. The diphtheria toxin causes inflammation of heart muscle (myocarditis) and this can lead to death if not treated with diptheria antitoxin and proper antibiotics. Formation of white-grey pseudomembrane over parts of the throat (pharynx) , voice box (larynx) and tonsils and swollen bull neck are considered stereotypical, although they may not show up in some cases.

Diphtheria is a vaccine preventable disease – the toxoid vaccine elicits an immune response against the toxin which is encoded by a tox gene of the pathogen. Sometimes, spurts of diphtheria outbreaks occur in unvaccinated or partially vaccinated communities.

There is an increasing trend in the number of cases of diphtheria globally, as the number of cases in 2018 (16,651) was double the 1996–2017 average (8,105). Relevant to India is the statistic that 50% of the cases that came up in 2018 were in India.

To understand the epidemiology of the disease from a genetic perspective, it is needed to know how the microorganism has evolved in time and over the geographical spread. It is needed to know whether the gene for antimicrobial resistance has evolved and to understand variants of the tox gene which may be prevalent thereby influencing the vaccine targeted towards toxin produced by an old strain of *C. diphtheriae.*

In order to map out the genetic spread of the organism, the group has done a phylogenetic analysis that basically gives a picture of the family tree of the species. Unlike certain other bacteria, *C. diphtheriae* has shown a diversity in evolution, which makes it, as a species, more stable and powerful. This is also true of clades (or groups) that are prevailing in India.

They then analyse the genes for their capacity towards antimicrobial resistance. Compared to the 1990s, isolates from the decade spanning the years from 2010 to 2019 show the highest average number of antimicrobial resistance genes encoding resistance for sulphonamide, aminoglycoside, chloramphenicol and trimethoprim.

“These antimicrobial resistance genes might have been transferred by the mobile genetic elements from other bacteria,” says Thandavaranyan Ramamurthy, one author of the paper. He is presently INSA-Senior Scientist at the ICMR-National Institute of Cholera and Enteric

Diseases, Kolkata, and the work was completed when he was at DBT-Translational Health Science and Technology Institute, Faridabad. “Fortunately, none of the isolates harboured beta-lactam resistance genes. [that is, for example, resistance to antibiotics like penicillin]. Penicillin or erythromycin are the choice of antibiotics for the treatment of diphtheria,” he explains.

Finally, the researchers study the variations (or mutations) in the tox gene, which is responsible for producing the diphtheria toxin – which is the main target of the vaccinations.

“We identified 18 tox gene variants, with mutations estimated in its toxin structural impact,” explains Dr. Ramamurthy. This may imply that specific vaccines made for a particular diphtheria toxin may not work against newly evolved ones. “However, this hypothesis has to be demonstrated in *in vitro* and *in* vivo studies,” he adds.

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The local mucosal immunity induced will likely reduce infection possibility and might prevent transmission

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