
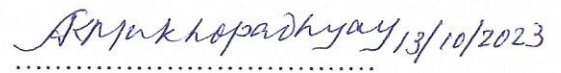


**A comparative study of virulence factors and antibiotic susceptibility pattern of enteric
Escherichia coli isolated from diarrheal patients.**

Abstract: Diarrhoea is mostly prevailing in developing countries, especially in Asia and Africa, where people suffer due to poor hygiene and limited healthcare facilities. According to the WHO report, diarrheal disease is the second leading cause of death in children under 5 years of age. One of the major causative agents of diarrhoea is *E. coli* which is prevalent in the human gastrointestinal tract as harmless commensals but can also turn to the pathogenic form on acquiring certain features by mobile genetic elements. Besides their prevalence, a major public health concern in diarrhoea endemic regions is the spread of antibiotic resistance (AMR) and the treatment has become more and more challenging due to the emergence of resistance against the first-line antimicrobial agents. Therefore, in this study, we targeted to analyze the prevalence and antimicrobial resistance of *E. coli* in diarrheal patients of Kolkata, India. We reported the presence of a large number (n=1153/14,613) of Diarrheagenic *E. coli* (DEC) such as EAEC, EPEC and ETEC along with EIEC during 2012-2022. Prevalence of EAEC was found more followed by ETEC, EPEC and EIEC in Kolkata among children which are interestingly different from the prevalence pattern of past decade. Antimicrobial susceptibility assay showed that the isolates have acquired increased resistance to fluoroquinolone group of antibiotics followed by β -lactams and tetracyclines. EIEC is found to be prevalent in Kolkata, India with two distinct forms LF and NLF. Most interestingly, the LF isolates which is a rare type of EIEC were found to coexist almost equally with the mostly studied NLF-EIEC strains. There is no previous study reporting the virulence of LF-EIEC isolates. Therefore, we extensively characterized the LF-EIEC and compared the pathogenicity between the two groups of EIEC showing that LF strains were more invasive and expressed the virulence associated genes at increased levels compared to the NLF-EIEC strains when tested on cultured mammalian cell-line. The LF strains were found to colonize more in the rabbit intestine and caused severe keratoconjunctivitis in guinea pigs. Plasmid profiling showed that the EIEC strains harboured multiple plasmids irrespective of NLF or LF forms which correlates with virulence. In another part, we isolated an EAEC strain that harbors *bla*_{NDM-1} gene conferring resistance to the carbapenem antibiotics, used as a last line of drug treating microbial infections. Therefore, this study also reports the first isolation of *bla*_{NDM-1} carrying EAEC in India and the *bla*_{NDM-1} carrying plasmid harbored multiple antibiotic resistance markers which can be threatening to the human population. We also investigated a bunch of fluoroquinolone resistant DEC strains for the presence of plasmid mediated quinolone resistance genes and nucleotide mutations in the chromosomal genes that are reported to contribute to quinolone resistance. However, no such novel mutation has been observed. Collectively, the findings of this study highlight the high prevalence of multidrug resistance in major DEC pathotypes that could be considered as the leading etiological bacterial agent responsible for diarrhea suggesting a significant public health threat and needs special attention. Also, monitoring the AMR surveillance needs special attention because the DEC isolates were highly resistant to commonly used antimicrobials in the treatment of diarrhea.


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Debjani Ghosh
(Ph.D. Candidate)


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(Supervisor)

Dr. Anish K. Mukhopadhyay
Scientist F (Sr. Deputy Director)
Division of Bacteriology
ICMR National Institute of Cholera and Enteric Diseases
P-33, C.I.T Road, Scheme XM
Kolkata-700010; India