

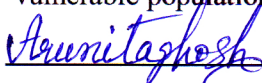
Title of thesis: **An Insight into the Epidemiology, *fimH* Gene Polymorphisms and Regulation of Phase Variation in Type 1 Fimbriae Operon of Drug-Resistant Uropathogenic *Escherichia coli* Isolated from Asymptomatic and Symptomatic Hospitalized Patients of Kolkata, West Bengal, India- A Molecular Perspective.**

## **ABSTRACT**

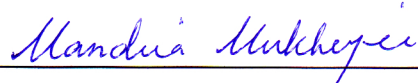
Uropathogenic *Escherichia coli* (UPECs), the predominant cause of all urinary tract infections (UTIs), can cause both asymptomatic Bacteriuria (ABU) and symptomatic UTIs. Symptomatic UTIs should be treated with antimicrobials to assuage symptoms and further complications, whereas ABU generally does not warrant treatment. However, the emergence of multidrug resistance (MDR) among pathogenic variants of *E. coli* isolated from asymptomatic and symptomatic patients represents a massive public health concern. Hence, the identification and characterization of ABU UPECs and their further comparison with symptomatic UPECs are an absolute necessity in the present era, for clinicians and microbiologists to devise strategies to combat their increasing pathogenicity.

In this study, the incidence of MDR and ESBL production was comparable among ABU (95%; 80%) and symptomatic (100%; 80%) UPEC isolates which were also statistically significant. The distribution of certain pathogenicity island markers, virulence factor genes,  $\beta$ -lactamase genes, mobile genetic elements (MGEs) and novel phylotype property (NPP) were also found to be significant among both groups. Clonal heterogeneity and predominance of ST940 (CC448) were evidenced among ABU and symptomatic UPECs; however zoonotic transmission was observed only in the former group. A close association between ABU UPECs with known and unidentified STs having NPPs with isolates that belonged to phylogroups Clade I, D, and B2 was observed. This study for the first time ventured to introduce a new approach to ascertain the phylotype property of the unassigned UPECs. Pathoadaptive FimH mutations, especially hot spot mutation V27A and MSHA was significantly prevalent among ABU UPECs, mostly reported in the symptomatic ones worldwide. The clinical ABU UPECs with remarkable adhesive capacity, unlike the prototype ABU strain but similar to symptomatic UPECs highlighted the incidence of bladder epithelial cell adherence in the case of individuals with ABU without manifestation of symptoms. Withal, this is the first study that attempted to investigate the regulatory interplay of three cellular factors; H-NS, IHF, Lrp on *fimB* and *fimE* recombinases that further domineered the inversion of *fim* switch and adhesive capacity among ABU UPECs. An association of V27A, N70S, and S78N FimH mutations with the higher adhesive capability and type 1 fimbrial expression was identified among both groups. Highly adherent UPECs regardless of their asymptomatic and symptomatic nature were mostly ESBL producers, harboured MGEs, and possessed NPP. These comparable characteristics of ABU and symptomatic UPECs might be attributed to the genome plasticity caused due to the deleterious effect of MDR.

Therefore, this study displayed the fact that ABU, although generally not considered as a clinical condition, their increased recognition, proper understanding, and characterization together with appropriate therapeutic measures when necessary is the need of the era which otherwise might lead to serious complications in the vulnerable population.

  
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