

TITLE: SPATES ARE POTENCIAL VIRULENCE FACTORS IN *ESCHERICHIA COLI* ISOLATED FROM BACTEREMIA

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ABSTRACT:

Extraintestinal pathogenic *Escherichia coli* (ExPEC) strains are the major cause of Gram-negative bloodstream infections. Although they are usually present in the normal intestinal microbiota, the acquisition of virulence factors-encoding genes allows the infection of extraintestinal sites. To succeed in the bloodstream they have to evade the host defenses. Serine protease autotransporters from Enterobacteriaceae (SPATEs) are secreted virulence factors involved in cytotoxic activities and interactions with components of the immune system. However, information regarding the presence of SPATEs encoding genes in ExPEC is scarce. Therefore, the aim of this study was to investigate the presence of SPATE-encoding genes in *E. coli* isolated from bacteremia. We selected 266 *E. coli* strains isolated from patients of both genders, various ages, and clinical conditions, in a public hospital in São Paulo (SP). The strains were kindly provided by Drs. A.C. Gales and A.C.Pignatary (ALERTA e LEMC-UNIFESP). SPATE-encoding genes were searched by PCR or DNA-DNA hybridization with specific probes. Phylogeny was assessed by Clermont's quadruplex-PCR. DNA-DNA hybridization was performed to assess intrinsic virulence (ExPEC⁺ or ExPEC⁻) by detection of *afa/dra*, *papA*, *papC*, *sfa/foc*, *iutA* and *kpsMT II*. Among all strains studied, 181 (68.04%) had at least one SPATE-encoding gene. *sat* (39.8%) was the most frequent, followed by *tsh* (35.3%), *vat* (33.1%), *pic* (8.3%), *espP* (1.9%), *espl*, *eatA*, *sepA*, *sigA* (1.1% each), *espC* (0.75%), and *pet* (0.37%); while *epeA* was not detected. Most of strains were ExPEC⁺ (60.9%). The distribution among phylogroups was: B2 (35.7%), E (16.2%), B1 (14.3%), A (11.6%), D (8.6%), F (8.3%), and C (3.4%). The frequency of SPATE⁺ExPEC⁺ was significantly higher than SPATE⁺ExPEC⁻ (56.4% \times 11.6%) showing an association between the presence of SPATE and intrinsic virulence ($p < 0.01$ Fischer exact test). Accordingly, SPATE⁺ strains were distributed more frequently among the virulent phylogroups B2, D, E, and F than SPATE⁻ strains (57.9% \times 10.9%). Corroborating the association of the SPATE genotype and more virulent phylogroups SPATE⁺ strains were statistically more frequent among the B2 group than SPATE⁻ isolates (33.8% \times 1.9%) ($p < 0.01$). Since some SPATEs are proteins with immunomodulatory activities, such as the cleavage of complement proteins, our data indicate that SPATEs may play an important role in the pathogenesis of bacteremia mediating evasion of the immune system.

Keywords: ExPEC, sepsis, SPATE, autotransporters.

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