

The Zoonosis Fingerprints in Bacterial Genome

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ABSTRACT

Extraintestinal pathogenic *Escherichia coli* (ExPEC) strains are diverse in nature and based on the host and the site of infection, different ExPEC strains cause different extraintestinal infections in humans, poultry, and dairy sector. Few of the *E. coli* isolates from milk and bovine feces have genetic similarities with human ExPEC i.e., they contain some ExPEC- associated virulence genes. These isolates are considered as potentially pathogenic that could be transmitted to humans and other animals through handling and/or consumption of contaminated raw milk and other milking equipment. However, the precise rate at which humans acquire ExPEC from bovine source via ingestion or management of ExPEC- contaminated foods, establish intestinal colonization, and ultimately develop infection at extraintestinal sites, remains unspecified and poorly understood. In this study, we assessed whether milk *E. coli* isolates from mastitic milk and fecal *E. coli* isolates from healthy lactating cattle could cause diseases in a chicken model of avian colibacillosis and two mice models of ExPEC-associated human infections (i.e., UTI and sepsis). Through whole generation sequencing (WGS), 110 bovine source *E. coli* isolates were categorized into ExPEC and non-ExPEC strains through screening for virulence genes associated with human-source ExPEC or avian pathogenic *E. coli* (APEC). Based on this screening, 8/ 23 *E. coli* isolates (34.8%) from mastitic milk and 6/87 *E. coli* isolates (6.9%) from fecal source were designated as ExPEC. The majority of these were further belonged to sepsis-associated *E. coli* (SEPEC) sub-pathotype (78.6%). The most prominent serotype and sequence type among ExPEC isolates was O15 (29%) and ST-69 (29%), respectively and most of the ExPEC isolates belonged to phylogroup D and A (29% each). Genetically identified ExPEC and non- ExPEC isolates selected for animal trials were assessed of antimicrobial resistance genes (AMRs) and stress genes as these genes can be transmitted to humans and other microbes through horizontal gene transfer. Multiple bovine-source fecal ExPEC isolates resembled avian and human clinical ExPEC isolates and few non-ExPEC isolates were evaluated in causing one or more ExPEC-associated illnesses in humans (UTI, sepsis) and chicken (colibacillosis) through experimental animal infection models. ExPEC isolates from milk and bovine fecal sources were able to cause UTI infection and lethal sepsis in mice models and the ExPEC isolates that resembled poultry-ExPEC isolates were also successful in causing colibacillosis in chicken models and showed high and intermediate pathogenicity index. While none of the isolates that were classified as non-ExPEC were able to cause ExPEC- associated illnesses in animal models. These findings suggest that *E. coli* isolates from bovine feces and raw milk that contain ExPEC-associated genes and exhibit ExPEC- associated *in vitro* phenotypes may pose a health threat to humans and other animals via zoonosis.

Keywords: ExPEC, Zoonosis, UTI, Bovine Feces, Raw Milk, SEPEC, APEC.