Dear Editor,

Shiga toxin-producing *Escherichia coli* (STEC) has long been considered as a major cause of bloody diarrhea, and a life-threatening condition named hemolytic uremic syndrome (HUS) in humans worldwide. Historically, the serotype O157:H7 STEC caused two large outbreaks in the United States and Japan in 1993 and 1996, respectively. This serotype has been frequently reported as a cause of diarrhea and HUS and therefore is the most investigated serotype worldwide. A brief search shows numerous reports of O157 *E. coli* in Iran among isolates from different animal species and occasionally humans—albeit not associated with severe cases. For instance, O157 *E. coli* has been reported in humans (uncomplicated diarrhea), sheep, goats, cattle, water buffalos and camels in Iran in recent years. At the same time, to the best of our knowledge, there has not been any outbreak reported in association with this serotype in humans in Iran. Accordingly, we can draw two hypotheses explaining this. First, it can be resulted from a lack of comprehensive monitoring that might need revising routine diagnostic algorithms, and the second could be the presence of less virulent clones of O157 *E. coli* circulating in Iran. With the context of the later hypothesis, we can explain this in brief as our current knowledge on virulence of this serotype increased substantially in the genomics era.

Based on the current knowledge, the O157:H7/H. *E. coli* belongs to a diverse group of *E. coli* showing different phenotypic and genotypic characteristics with substantial variations in virulence of the bacterium. One of the first variants was the sorbitol fermented O157 *E. coli* (SF O157) that was also associated with sever diseases. In addition, the polyphyletic evolutionary events occurred within each serogroup caused more complexity resulting O157 *E. coli* belonging to different clonal complexes (CC). Recent advances in genomic analysis and use of wider genomic typing approaches like single nucleotide polymorphism (SNP) analysis revealed at least 9 clades in O157: H7 *E. coli*. Comprehensive studies revealed that only a subset of O157 *E. coli* exhibit high virulence that is mostly seen in clades 8 and 6. Some factors seem to be associated with enhanced virulence, of which production of higher levels of Shiga toxins is the best understood. Highly virulent O157 strains usually harbor stx2a and/or stx2c subtypes. The stx2c is highly homologous and the main contributor is supposed to be Stx2a produced by the host strain. Based on sequence variations and integration site of lambdoid phages, Shiga toxin-encoding prophages can be divided into different genotypes/subtypes. In the highly pathogenic clade 8, two types of Stx2a encoding phages were found, of which one (subclade 8a) produce higher level of Stx and is supposed to be more virulent because it was mostly associated with HUS cases.

On the other hand, some O157 strains are not toxigenic – and are negative for stx genes. Nevertheless, such strains should not be considered non-virulent because of the mobile nature of stx gene carried by phages that may result in gain and loss of stx. The shared sequence types (ST) between STEC and enteropathogenic *E. coli* (EPEC) strongly suggest some stx-negative O157 strains to be the progenitors of STEC (pre-STEC) or strains that lost Shiga toxin genes (STEC-LST).
Most reports on O157:H7 *E. coli* in Iran lacks detailed analysis and simply shows the existence of this serotype in population without particular attention to other important genotypic characteristics such as stx subtypes, phage integration sites, intimin subtypes or other phenotypic traits like sorbitol fermentation or Stx production. Recent comparative studies on O157:H7 strains isolated from different geographical areas and countries showed that this serotype was first spread and then was subjected to divergent evolutionary events that resulted in genotypic variations in different geographical areas. Such evolutionary changes may have occurred in Iran or elsewhere with unknown effects on virulence depending on the genomic composition. In conclusion, studies on STEC serotypes in Iran should not be confined to O157:H7 and more importantly, the simple report of O157 *E. coli* seem to be uninformative epidemiological finding without clarifying more details of such strains and validation of results by a reference laboratory.

**Conflict of Interest Disclosures**

None.

**References**