

Streptococcus equi subspecies *zooepidemicus* as an Emerging Zoonotic Pathogen of Public Health Significance

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Emerging and re-emerging zoonotic pathogens, which include viruses, bacteria, fungi, and parasites are important causes of morbidity as well as mortality in humans and a wide variety of animals; and are transmitted through various routes [1-3]. The bacteria that belong to genus *Streptococcus* are gram positive, non-motile, non-sporulated, catalase positive, oxidase negative, facultative anaerobes, and grows well on blood agar [4]. There are several species of *Streptococcus* including *S. pneumoniae*, *S. pyogenes*, *S. equisimilis*, *S. suis*, *S. agalactiae*, which are implicated in various clinical disorders of humans and animals [2,4-7].

Streptococcus equi subsp. *zooepidemicus* (SEZ), which belongs to beta-hemolytic group C *Streptococcus*, occurs as a commensal in equines, and also can act as an opportunistic pathogen under immunosuppression or stress resulting infections in animals [8]. There are several virulence factors, such as capsule formation, M-like proteins, exotoxins, and adhesins, which can facilitate colonization, and immune evasion besides systemic dissemination [9].

Natural infections due to SEZ have been recorded in several species of animals including horses, pigs, dogs, cats, donkeys, cattle, sheep, monkeys, Guinea pigs, and humans [8,10-14]. The increasing reports of human infections is a clear indication of emerging zoonotic significance of this bacterium. Outbreaks have been described in humans, horses, pigs, sheep, cats, and dogs [10,12,14-16].

Humans can acquire the infection by direct contact with infected animals, especially horses [16]. Consumption of unpasteurized milk or dairy products can also result in infection [8,17]. An outbreak of *Streptococcus equi* subspecies *zooepidemicus* linked to with ingestion of fresh goat cheese was reported by Kuusi and others [15]. Likewise, Bosica and co-investigators [18] described 32 cases of SEZ in humans in Italy during November 2021 to May 2022. The epidemiological investigation and molecular studies indicated that consumption of unpasteurized fresh dairy products was the source of the outbreak. It is pertinent to state that pasteurization of milk plays a vital role to break the transmission cycle of SEZ infection.

Occupational groups, such as veterinarians, equine handlers, farmers, and animal attendants are at higher risk of acquiring the infection. Most cases are associated with occupational exposure to horse, and also ingestion of unpasteurized milk and milk products [16]. Transmission of SEZ from horses to humans was investigated by Pelkonen and co-workers [16]. Detailed molecular typing showed that both animal and human isolates showed similarity thus confirming the zoonotic potential of SEZ.

In humans, SEZ causes pneumonia, meningitis, endocarditis, nephritis, glomerulonephritis, arthritis, and streptococcal toxic shock-like syndrome [16,19]. The patients suffering from meningitis have mortality, and develop severe complications like hearing loss [19]. During an outbreak of SEZ in Italy, Buscia and co-investigators [18] recorded wide range of clinical symptoms, such as fever, diarrhoea, headache, vomiting, septicaemia, cystitis, and pharyngitis in persons who drank unpasteurized dairy product.

A wide variety of symptoms, such as endometritis, pneumonia, mastitis, respiratory disorders, arthritis, and septicemia have been observed in animals [10,11,14].

Bacteriological (culture), and molecular (PCR) techniques are employed to establish the diagnosis. The isolation of the bacterium from clinical specimens can be attempted on blood agar. Biochemical tests are performed for the identification of bacterium. PCR is considered more sensitive than conventional culture, particularly in carrier animals [20]. In this context, Kinoshita, *et al.* [21] mentioned that advanced technique like loop-mediated isothermal amplification (LAMP) provides rapid detection of the organism.

Penicillin remains the mainstay for the treatment of SEZ infections [17,22]. In this context, Byun and co-workers [23] reported that canine isolates of *S. zooepidemicus* were found to be susceptible to penicillin, ampicillin, amoxicillin, and enrofloxacin. Another study conducted by Nocera and co-investigators [22] described that third generation cephalosporins, such as ceftiofur and ceftriaxone, were highly effective. The findings of these studies suggested that other antibiotics, such as ampicillin, amoxicillin, enrofloxacin, ceftiofur, and ceftriaxone can be used as an alternative therapy. In severe cases, combination therapy and supportive care like oxygen supplement, and fluid replacement are required to mitigate the suffering of the patients [17]. It is pertinent to state that emerging resistance demands antimicrobial susceptibility test before instituting therapy [8,17]. It is suggested that early correct diagnosis and prompt treatment is imperative to prevent the morbidity and mortality.

Currently, there is no vaccine that is commercially available for SEZ infections, and therefore, certain measures, such as pasteurization of milk and dairy products, isolation of infected animals, hygiene and biosecurity in animal handling, personal proactive wear for high-risk groups like veterinarians, animal handlers, equine owners, and enhanced surveillance are helpful in the prevention and control of SEZ infections [15,16,18,24,25].

It is concluded that *Streptococcus equi* subsp. *zooepidemicus* is an emerging, life-threatening bacterial zoonotic pathogen with growing global importance. The infection can occur in sporadic as well as epidemic form, and is reported from many countries of the world. It is recommended that better diagnostics, robust surveillance, and public cognizance about the source of infection, mode of transmission, and preventive strategies are crucial to diminish its effect on human and animal health. The implementation of One Health approach by including experts from various disciplines like veterinary, medical, and environment, is imperative to control this emerging zoonotic pathogen. It is emphasized to conduct further studies to elucidate the etiologic significance of SEZ in various clinical disorders of humans and animals.

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