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Neglected parasite of rats and mice: *Cryptosporidium*

Neslihan Ölmez[1]*, Barış Sarı[1]

[1]Kafkas University, Faculty of Veterinary Medicine, Department of Parasitology, Kars, Türkiye

*Corresponding: neslihan_gunduz@hotmail.com

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Abstract
Cryptosporidium spp. is an important zoonotic intestinal pathogen that can cause gastrointestinal symptoms and trigger the hosts immune response. *Cryptosporidium* species can infect humans and more than 260 animal species, including 54 rodent species. This review provides a comprehensive review of the pathogenesis, clinical symptoms, diagnostic methods, treatment approaches and prevention strategies for disease control of *Cryptosporidium* species infecting rats and mice. The pathological effects of the known pathogenic species *C. muris* and *C. parvum* and their role in rats and mice are discussed. The importance of prevention methods such as hygiene measures and biological safety practices are emphasized to control the disease. Cryptosporidiosis poses a serious threat to both animal health and public health and therefore the development of effective prevention strategies is essential.

Keywords: *Cryptosporidium spp., mice, parasites, rat*

1. Introduction

Cryptosporidiosis is a zoonotic disease caused by *Cryptosporidium*, which can infect a variety of hosts, including rodents such as mice and rats. Numerous studies have investigated the prevalence of *Cryptosporidium* spp. in mice and rats, particularly emphasizing their role as potential reservoirs for this zoonotic pathogen. In laboratory studies in mice and rats, the presence of possible *Cryptosporidium* infection can affect the research in multiple dimensions. The effects of the disease are multidimensional and can affect important data such as experimental design, contamination risks, and interpretation of results.

Multiple species have been molecularly detected in mice and rats, including *Cryptosporidium parvum*, *C. muris* and *C. tyzzeri*, with at least three species detected in mice and five different species in rats, with *C. tyzzeri* being particularly notable in mice.[1] *C. parvum* is recognized for its zoonotic potential, underscoring the public health implications of these findings.[2,3]

Urban and peri-urban environments facilitate the potential for zoonotic transmission by providing ideal conditions for interaction between humans and these rodent reservoirs. The proximity of rodent populations to human habitats increases the risk of infection, especially in areas with poor hygiene.[4,5] Furthermore, the detection of *C. muris* in various rodents highlights the ecological adaptability of *Cryptosporidium* and supports the notion that rodents are important reservoirs of these parasites.[6,7] *Cryptosporidium* has been detected in various rodent species with variable prevalence rates; 8.0-31.4% in mice, 0.8-73.0% in gerbils and 2.1-63.0% in rats,[3] 3.2-2.1% of the bamboo rats,[8,9] rodents 34.46%.[10] The infection rates of *Cryptosporidium* in laboratory rodents from different regions of China were 4.3%, 12.0%, and 2.3% respectively.[7]

Laboratory rodents are widely used in medical, biological, pharmacy, animal husbandry, veterinary medical and scientific research.[7] When *Cryptosporidium*-infected mice and rats are used in research, findings on disease mechanisms or treatment efficacy may be confounded, leading to inaccuracies in data on host responses or pathogen interactions.[11,12]

Agents Causing Cryptosporidiosis in Mice and Rats

1.1. Cryptosporidium muris

Morphology &Biology

Two different species of *Cryptosporidium* spp. belonging to the family Cryptosporidiidae have been reported to infect mice: *C. muris* and *C. parvum*. The oocysts of *C. muris* measure 5.3µ x 7.9µ. The sporulated oocyst contains four naked sporozoites.[13-15]

Cryptosporidium muris or *C. muris*-like coccidia have been reported in many mammals. Recent morphological and phylogenetic analyses have shown that *C. muris* is not a uniform species and that isolates infecting rodents probably constitute a distinct species from those infecting large mammals. *Cryptosporidium muris* has been found in wild mice and rats worldwide and reports from laboratory colonies are rare.[13]

Cryptosporidiosis occurs by oral ingestion of oocysts from contaminated feed and water. Sporozoites released in the stomach infect the glandular gastric epithelium. Intracellular, extracytoplasmic *C. muris* lives in

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the parasitophorous vacuole just beneath the host cell membrane. *Cryptosporidium muris* undergoes sexual reproduction and multiple schizogony. Oocysts sporulate and become infective before being expelled by the host. Some of these oocysts are thin-walled and rupture in situ, causing the infection to intensify and recurrent autoinfection. The prepatent period lasts approximately 10 days.[13,14]

1.2. Cryptosporidium parvum

Morphology &Biology

Oocysts of *C. parvum* are smaller than those of *C. muris*, are ovoid to spherical, and measure 4µ to 5µ by 3µ. *Cryptosporidium parvum* infects all mammalian species, including rodents and humans, and causes more severe infections, especially in neonatal and immunocompromised hosts. *C. muris* infects the gastric glands, while *C. parvum* infects the microvilli region of the small intestine, particularly the ileum. In immunocompromised adult rodents, infections are mild and the animals recover rapidly. While immunocompetent hosts show no clinical signs, experimentally infected neonates, patients with severe combined immunodeficiency (SCID), and other immunocompromised or immunosuppressed mice and rats develop a severe and fatal chronic infection characterized by diarrhea, dehydration, and depression, with infection of the ileum, cecum, and colon.[13,14]

2. Clinical Disease, Diagnosis and Treatment

It causes chronic gastric cryptosporidiosis and leads to symptoms such as diarrhea, weight loss, and in severe cases, dehydration.[16,17] The oocysts can be observed in feces and are typically detected using staining techniques such as the modified acid-fast stain or other specific immunological assays[10,13,18] and by molecular methods.[14]

Nitazoxanide is one of the few pharmacologic agents that has proven effective against *Cryptosporidium* in clinical cases. In one study, nitazoxanide effectively eliminated *C. parvum* oocysts in healthy volunteers, but more research is needed to determine its specific effects on *C. muris.*[19] Immune-mediated responses, particularly T cell-mediated immunity, have been implicated in cryptosporidiosis in immunocompetent hosts.[20] In particular, CD4+ and CD8+ T lymphocytes have been shown to play an important role in controlling infection and facilitating recovery.[16] Furthermore, feeding certain diets or probiotics can influence the severity of *Cryptosporidium* infections, thus indicating the need for nutritional management in laboratory settings.[21,22] For instance, metabolic analyses have shown that dietary fiber deficiency increases susceptibility to *Cryptosporidium* infections in mice.[21]

3. Prevention

Research has shown that gastrointestinal microbiota influence the severity of *Cryptosporidium* infections, suggesting that differences in microbiota composition between different laboratory animals may lead to inconsistent research results.[23] This suggests the need to standardize the health status of laboratory animals before conducting experiments.

Cryptosporidium parvum is a zoonotic parasite that can cause serious infection, especially in immunosuppressed individuals. All personnel working with rodents known to be infected with this parasite should wear personal protective equipment and follow standard operating procedures for hygiene and personal protection. Persons known or suspected to be immunocompromised should not work with rodents infected with *C. parvum.*[13]

In conclusion, there is strong support for the role of mice and rats as key reservoirs for *Cryptosporidium* spp. with important public health implications. The focus on *Cryptosporidium* has increased over the past few years with studies of treatment and potential vaccines. With this increased interest, it is crucial that researchers continuously monitor the health status of rodent populations and implement strict biosecurity measures to minimize contamination risks. Insufficient attention to these factors may lead to an underestimation of the epidemiological importance of *Cryptosporidium* in laboratory settings.

Studies have shown that wild and commensal rodents serve both as carriers to other species and as potential sources of infection for humans.[12] Therefore, epidemiologic understanding of cryptosporidiosis in rodents is critical for developing effective control strategies and informing public health policies.

Ethical approval

This study does not require approval from the Ethics Committee for Animal Experiments.

Authors contribution

NÖ; Investigated and designed the review, analysed the data wrote the original drafting. BS; Investigated and designed the rewiew, confirmed the data, edited and finalized the draft. All authors have read and approved the final version of the manuscript.

Conflict of interest

There are no conflicts of interest associated with this re-search publication, according to the authors.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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