

**LETTER TO EDITOR**

**Molecular Detection of *Leptospira* in Pediatric Aseptic Meningitis**

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**ABSTRACT**

Leptospirosis is a zoonotic disease caused by pathogenic *Leptospira* bacterial species. It is tremendously neglected, and scarce epidemiological data is present worldwide. Aseptic meningitis is a rare secondary manifestation of *Leptospira* infection. Molecular detection of leptospira DNA in cerebrospinal fluid (CSF) samples of children younger than two years is could be considered for diagnosis of aseptic meningitis.

A total of 50 CSF samples suspected of aseptic meningitis were collected from pediatric patients (<2 years) presenting to Omdurman Teaching Hospital in Khartoum state, Sudan, between June and September 2018. PCR was used to investigate the presence of leptospira DNA in these samples.

Out of the 50 CSF samples in our study, two samples (4%) tested positive for *Leptospira* DNA using PCR. *Leptospira* is an overlooked cause of aseptic meningitis in children, and PCR can be used for its diagnosis. *J Microbiol Infect Dis* 2022; 12(1):35-37.

**Keywords:** *Leptospira*, pediatric, aseptic meningitis, diagnosis, molecular

Dear Editor,

In this study, a total of 50 samples suspected of aseptic meningitis were collected from pediatric patients (<2 years) presenting to Omdurman Teaching hospital in Khartoum state, Sudan, during the period between June and September 2018. PCR was used to investigate the presence of leptospira DNA in these samples. Out of the 50 CSF samples in our study, two (4%) tested positive for *Leptospira* DNA using PCR. It is concluded that leptospirosis should be suspected in any case of meningitis of unknown origin. PCR can be used for its rapid and accurate diagnosis in Sudan.

Leptospirosis is a zoonotic disease caused by pathogenic *Leptospira* bacterial species [1]. It is tremendously neglected, and scarce epidemiological data is present worldwide [2]. The clinical picture of leptospirosis is diverse, with a broad spectrum of manifestations, ranging from a mild febrile illness to life-

threatening fulminant disease. It is transmitted to humans principally via environmental water contaminated with the urine of wild and domestic mammals that *Leptospira* chronically colonizes. Aseptic meningitis is a rare secondary manifestation of *Leptospira* infection [3]. Leptospirosis can cause aseptic meningitis during the second (immune) phase of the illness and is typically associated with uveitis, rash, conjunctival suffusion (which differentiates it from others), adenopathy, and hepatosplenomegaly [1,4,5]. Typical findings on CSF examination include a lymphocytic predominance with total cell counts of up to 500/mm<sup>3</sup>, protein levels between 50 and 100 mg/ml, and normal glucose levels, consistent with aseptic meningitis [6]. The most common approach used for the diagnosis of leptospirosis was the detection of antibodies using Enzyme-Linked ImmunoSorbent Assay (ELISA) or Microscopic agglutination test (MAT). However, various molecular techniques, including conventional and real-

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time polymerase chain reaction (PCR), have been developed for the specific detection of pathogenic bacteria from the genus *Leptospira* [7]. Leptospiral meningitis is never suspected in cases of aseptic meningitis in Sudan. Several studies have concluded that leptospirosis is endemic in both animals and humans in Sudan using serological and molecular techniques. The disease could be considered one of the causes of human renal failure [8-10]. Therefore we set out to probe the possibility of this infection in aseptic meningitis Sudanese patients using the PCR technique described by Hookey, 1992 [11].

In a cross-sectional study, a total of 50 CSF samples (30 males and 20 females) suspected of aseptic meningitis were collected from pediatric patients (age less than two years) presenting to Omdurman Teaching Hospital in Khartoum state, Sudan, during the period between June and September 2018. The patient was of different ages and was selected on the basis of first come, first enrolled. According to the manufacturer's protocol, bacterial DNA from these CSF samples was extracted using QIAGEN Mini Kit [Germany] and tested by PCR. Out of the 50 CSF samples in our study, two (4%) tested positive for *Leptospira* DNA using PCR. The two patients were males, aged 5 and 6 months, respectively. No association with clinical data or demographics was found. The source of infection is unknown. However, in a study that was done in the Netherlands between 2011 and 2014, 19 patients with leptospirosis were identified [12]. Seven (37%) underwent a lumbar puncture for suspected meningitis, of which six had been in contact with fresh water in a tropical area. Four of these seven patients (57%) with suspected meningitis had cerebrospinal fluid pleocytosis indicative of leptospiral meningitis and presented with headache, fever, and neck stiffness. The authors recommended that leptospiral meningitis should be considered in the case of suspected meningitis and history of visiting tropical areas or direct or indirect contact with animal urine. A cerebrospinal fluid examination is vital for the differential diagnosis of leptospirosis. The authors also stated that the outcome was generally favorable in patients with leptospiral meningitis treated with antibiotics [12].

A similar study was done in Brazil to investigate leptospirosis as the cause of

aseptic meningitis using different diagnostic techniques, including the polymerase chain reaction (PCR) in Thirty-nine cerebrospinal fluid (CSF) samples from patients presenting with meningeal abnormalities with a predominance of lymphocytes and negative results by traditional microbiological tests. *Leptospira* spp DNA was detected in 23 (58.97%) CSF samples. Leptospirosis could be detected by PCR assay from the 3<sup>rd</sup>-26<sup>th</sup> day after illness onset. The sensitivity of the PCR was assessed with confirmed cases of leptospirosis (by MAT) and found to be 89.5%. All CSFs used in this study were negative by culture. The study recommended that PCR be used as a supplementary diagnostic tool, especially in the early stages of the disease, when other diagnostic techniques such as serology are not sensitive [13].

Our study clearly showed that *Leptospira* is an overlooked cause of aseptic meningitis in children in Sudan. It is recommended that it should be considered in any case of meningitis of unknown origin, and PCR can be used for its rapid and accurate diagnosis in Sudan. This study also calls for further, more extensive studies on this subject, especially in rural areas of Sudan.

To the best of our knowledge, this is the first study to confirm leptospirosis as a possible cause of aseptic meningitis in Sudan. This study is intended to alert physicians that it would seem useful to consider the possibility of leptospiral infection for any case of meningitis of unknown origin. This study aims to alert the local authorities about this neglected public health hazard, especially since leptospirosis is endemic in many rural and urban communities in Sudan.

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