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RESEARCH LETTER

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Congenital babesiosis in China: first molecularly confirmed case of vertical transmission of *Babesia microti*

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ABSTRACT

Congenital babesiosis is rarely reported globally. We report a 74-day-old male infant presented with fever, pallor, and severe, life-threatening haemolytic anaemia (haemoglobin: 45 g/L). The infant had 16% parasitemia with ring forms evident on peripheral blood smear. *Babesia microti* infection was confirmed in both the mother and infant by PCR and metagenomic next- generation sequencing. Genetic analysis revealed an identical strain in bot. Treatment with intravenous azithromycin and oral atovaquone/proguanil resulted in rapid clearance of parasitemia and resolution of anaemia. This first molecularly confirmed case of congenital *B. microti* transmission in China demonstrates vertical transmission from an asymptomatic mother. It underscores the need for heightened clinical suspicion in neonates with unexplained haemolytic anaemia in endemic regions and highlights critical gaps in access to essential anti-babesia therapies.

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KEYWORDS Congenital babesiosis; Infant; *babesia microti*; Atovaquone-proguanil

Human babesiosis is an emerging infectious disease worldwide caused by intraerythrocytic protozoan parasites of the genus *Babesia* [1]. Transmission typically occurs through tick bites, blood transfusion, organ transplantation, or vertical (maternal-infant) transmission [2]. While many *Babesia* infections are mild or asymptomatic, severe disease can occur in infants, the elderly, asplenia individuals, and immunocompromised patients [3]. The disease can present with clinical manifestations such as fever, jaundice of the skin and mucous membranes, and haemoglobinuria [4]. *Babesia* has a global distribution. Since Romanian scientist Babes first discribed *B. bigemina* in the red blood cells of diseased cattle in 1888, over 100 species have been identified and reported. However, only four species are recognized as established human pathogens, primarily *B. microti*, *B. divergens*, *B. duncani*, and *B. venatorum*. Following the first reported case of human babesiosis by Yugoslav scholars in 1957, cases have been documented in the Americas, Europe, Asia, Africa, and Oceania, with the highest numbers occurring in the Americas and Europe. Since babesiosis became a nationally notifiable disease in the United States in 2011, approximately 1,000 cases have been reported annually, predominantly caused by *B. microti*. Reported cases exceeded 2,000 in 2020, marking a historic high [5]. Europe reports relatively fewer cases, *B. divergens*, *B. venatorum*, and *B. microti* being the principal pathogenic species. In recent years, countries including Egypt, Mexico, South Africa, Mozambique, Australia, Brazil, Japan, and South Korea have also reported human *Babesia* infection [6].

A retrospective analysis was conducted on human *Babesia* infections reported in China from 1943 to 2025. The first documented case of babesiosis in China occurred in 1943. In total, 324 cases of human babesiosis and/or asymptomatic infections were reported during this period (Chinese CDC surveillance data). These cases were distributed across 17 provinces/municipalities, including Heilongjiang, Guangxi, Henan, Inner

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Mongolia, Xinjiang, Gansu, Beijing, Chongqing, Shandong, Fujian, Zhejiang, Jiangsu, Jiangxi, Guangdong, Yunnan, Sichuan and Taiwan. The highest numbers of reported cases were from Heilongjiang, Henan, Yunnan, and Guangxi, showing a northeast-to-southwest distribution pattern. The primary infecting species include *B. microti*, *B. venatorum*, *B. divergens*, *B. crassa*-like, *B. microti*-like.

Recently, a 74-day-old male infant was admitted with pallor and fever (38.6°C) to a local hospital and was transferred after failing to improve following 20 days of inpatient care (Figure 1(A)). Laboratory tests revealed severe haemolytic anaemia, with haemoglobin 45 g/L (normal: 99–196 g/L), reticulocyte count 18.71% (normal: 0.5–1.5%), total bilirubin 30.04 μmol/L (normal: 3.4–17.1 μmol), direct bilirubin 10.4 μmol/L (normal: 0–6.8 μmol/L), indirect bilirubin 19.64 μmol/L (normal: 1.7–10.2 μmol/L), and lactate dehydrogenase (LDH) 1346.24 U/L (normal: 109–245 U/L). After 20 days of treatment without improvement in haemoglobin level, the infant was transferred to Children's Hospital of Fudan University for further evaluation. Upon transfer, the infant's laboratory values showed haemoglobin 57 g/L, haematocrit 20.9% (normal: 29–57%), reticulocyte count 23.0%, and red blood cell count 1.84×10^{12}/L (normal: 3.5×10^{12}/L to 5.6×10^{12}/L). Re-examination of bone marrow smear from the early stage of illness revealed ring-shaped parasites within erythrocytes (Figure 1(B)). On hospital day 5, peripheral blood smears again demonstrated intraerythrocytic parasites with characteristic ring forms, and parasitemia was quantified at 16% (Figure 1(C)). High-throughput metagenome sequencing of venous blood confirmed the presence of *Babesia microti*. To further support the diagnosis, nested PCR targeting the 18R rRNA gene was performed on blood samples from both the infant and the mother, both yielded positive results (Figure 1(D)). Phylogenetic analysis showed that the sequences obtained in this study clustered with reference *B. microti* sequences on the same branch. (Figure 1(E)). Furthermore, immunological testing of the mother's serum was positive for *Babesia* IgG, indicating prior exposure.

The mother of the child is 34 years old, in good health, and denies any history of tick contact. Given that the infant was born in January, a winter month with low temperatures, he had minimal outdoor activity, wore thick clothing, and no tick bites reported. The high genetic similarity of the *B. microti* sequences obtained from both the infant and the mother, strongly support vertical transmission. Therefore, the final diagnosis was *B. microti* infection acquired transplacental from the mother. The recommended treatment regimen domestically and internationally is intravenous antibiotics (azithromycin/clindamycin) combined with antiparasitic therapy (such as atovaquone-proguanil or quinine). Since antiparasitic medications are not readily available in mainland China, azithromycin was administered initially while atovaquone/quinine was being procured. The infant received intravenous azithromycin (10 mg/kg daily) and packed red blood cell transfusions. On hospital day 14, oral atovaquone/proguanil hydrochloride (0.5 capsules every 12 h) was initiate after the medication was obtained from Hong Kong. Two days later, parasitemia decreased to 13%, and after eight days of oral therapy, it further declined to 6%. Initially, RBC count, haemoglobin, and haematocrit were markedly reduced. Following two blood transfusions (on days 2 and 11), these indices improved transiently but subsequently decreased again. After six days of o atovaquone/proguanil therapy, a third transfusion was performed， and RBC count, haemoglobin, and haematocrit gradually increased and stabilized. Although hepatosplenomegaly persisted, and high-throughput sequencing continued to detect *B. microti,* the infant was discharged on the 24t of hospitalization. And follow-up 11 days later, no parasites were seen on blood smear. After two months, hepatomegaly had improved, and *B. microti* was no longer detectable by high-throughput sequencing (which offers higher sensitivity for detecting residual DNA than PCR). The infant has remained healthy during subsequent follow-up.

Infants with transplacental babesiosis typically present with nonspecific findings, including fever, irritability, poor feeding, pallor, and hepatosplenomegaly, between 3 and 6 weeks of age [7]. Vertical transmission serves as a significant non-vector-mediated route of *B. microti* transmission in natural reservoir host, however, because of its rarity and absence of specific clinical features, babesiosis is often not initially considered in neonates [8]. This case underscores the potential benefit of screening pregnant women in endemic areas and close postnatal monitoring of infants born to mothers with babesiosis for possible transplacental infection.

According to current literature, fewer than ten cases of *Babesia* infection worldwide have been definitively attributed to mother-to-child transmission (vertical transmission) [2,7,9–15]. Representative reports include the first confirmed case of transmission in 1987, in which a mother acquired *B. microti* via a tick bite during pregnancy, and the infant presented with fever and pallor at one month of age, with diagnosis confirmed by blood smear and serologic testing [9]. Another notable case involved a 44-year-old woman who developed babesiosis at 35 weeks of gestation. Following an emergency cesarean section, she delivered twin boys, and ring-form parasites were identified in the blood smear of one neonate, with *B. microti* infection subsequently confirmed by PCR [14].

Although cases of babesiosis have been reported in China, this is first molecularly confirmed case of vertical transmission of *B. microti* in the country. This case in China highlights the importance of heightened clinical awareness and diagnostic vigilance in infants

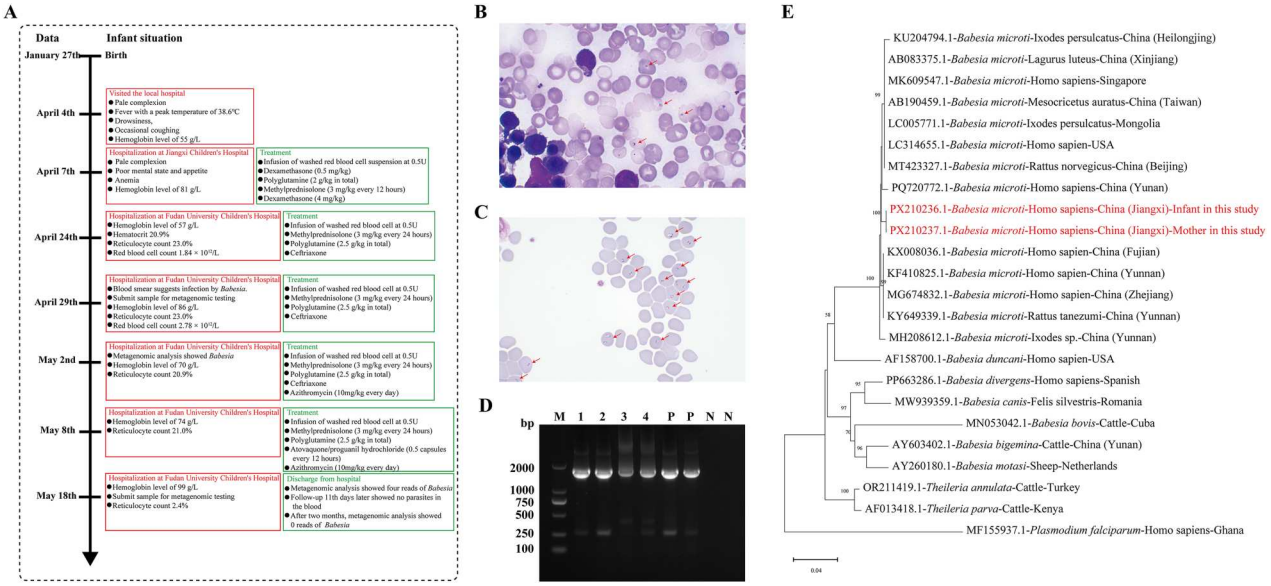


Figure 1. Clinical course and detection of *Babesia microti* in the infant and mother. (A) Key changes in the patient's haematological and biochemical parameters and corresponding therapeutic following disease onset. (B) Bone marrow smear from the infant showing ring forms of *B. microti* within red blood cells (indicated by red arrows). (C) Peripheral blood smear from the infant showing ring-form trophozoites of *B. microti* within red blood cells (indicated by red arrows). (D) PCR amplification results demonstrating *B. microti* DNA in blood samples from the infant (lanes 1 and 2) and the mother (lanes 3 and 4), P: positive control, N: negative control. (E) Molecular phylogenetic analysis of apicomplexan parasites based on partial amino acid sequences of small subunit ribosomal RNA (18S rRNA) gene. The phylogenetic tree was constructed using the neighbour-joining method implemented in MEGA software (version 12, https://www.megasoftware.net/). Brance support was evaluated by bootstrap analysis with 1000 replicates. The scale bar represents 0.04 substitutions per site.

with unexplained haemolytic anaemia, particularly in endemic regions. Strengthening serological screening for *Babesia* during pre-pregnancy and prenatal care help identify maternal infections early and ensure timely intervention for newborns at risk. Moreover, the diagnostic and treatment process in this case underscores limited clinician awareness, the absence of standardized diagnostic assays, and restricted access to effective antiparasitic medications in China. These gaps may contribute missed diagnoses, delayed treatment, and an increased risk of adverse outcomes.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The datasets used during the current study are publicly available, and were also available from corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Children's Hospital of Fudan University.

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