REPORT OF HUMAN FASCIOLIASIS UNDER DIFFERENT CLIMATIC CONDITIONS IN BRAZIL

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ABSTRACT: Introduction: Human fascioliasis is a plant-borne and water-borne infection caused by the trematodes *Fasciola hepatica* and *Fasciola gigantica*. It is one of the main neglected tropical diseases, and infections in humans occur via the ingestion of contaminated water and food. This study reviews all the recorded cases of human fascioliasis in Brazil under different climatic conditions in the national territory. Methodology:A survey of human fascioliasis cases in Brazil was carried out using the Google Scholar, Lilacs and PubMed databases. The climatic variables such as temperature, precipitation, moisture and altitude were obtained from the database of the Instituto Nacional de Meteorologia (INMET). Results: Between the years 1958 and 2022, sixty-six cases of human fascioliasis were recorded in places with temperature levels between 22 °C to 33 °C, humidity 78% to 86%, precipitation 90 mm to 167 mm, and at an altitude of 16 to 935 meters above sea level. Conclusion: The parasite's ability to adapt to different climatic conditions is observed in Brazil and the number of cases of human fascioliasis in the national territory may be higher due to underreporting related to the difficulty in diagnosing the infection.

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KEYWORDS: Fascioliasis; Fasciola Hepatica; Trematoda; Weather; Neglected Zoonosis.

REGISTRO DE FASCIOLOSE HUMANA EM DIFERENTES CONDIÇÕES CLIMÁTICAS NO BRASIL

RESUMO: Introdução: A fasciolíase humana é uma infecção de origem vegetal e hídrica, causada pelos trematódeos *Fasciola hepatica* e *Fasciola gigantica*. É uma das principais doenças tropicais negligenciadas, e as infecções em humanos ocorrem através da ingestão de água e alimentos contaminados. Este estudo revisa todos os casos registrados de fasciolíase humana no Brasil sob diferentes condições climáticas no território nacional. Metodologia: Um levantamento dos casos de fasciolíase humana no Brasil foi realizado nas bases de dados Google Scholar, Lilacs e PubMed. As variáveis climáticas como temperatura, precipitação, umidade e altitude foram obtidas do banco de dados do Instituto Nacional de Meteorologia (INMET). Resultados: Entre os anos de 1958 e 2022, sessenta e seis casos de fasciolíase humana foram registrados em locais com níveis de temperatura entre 22 °C a 33 °C, umidade de 78% a 86%, precipitação de 90 mm a 167 mm e altitude de 16 a 935 metros acima do nível do mar. Conclusão: A capacidade de adaptação do parasito a diferentes condições climáticas é observada no Brasil e o número de casos de fasciolíase humana no território nacional pode ser maior devido à subnotificação relacionada à dificuldade de diagnóstico da infecção.
PALAVRAS-CHAVE: Fasciolíase; Fasciola Hepatica; Trematódeos; Clima; Zoonose Negligenciada.

REGISTRO DE FASCIOLIASIS HUMANA BAJO DIFERENTES CONDICIONES CLIMÁTICAS EN BRASIL

RESUMEN: Introducción: La fascioliasis humana es una infección de origen vegetal y acuático, causada por los trematodos Fasciola hepatica y Fasciola gigantica. Es una de las principales enfermedades tropicales desatendidas, y las infecciones en humanos ocurren a través de la ingestión de agua y alimentos contaminados. Este estudio revisa todos los casos registrados de fascioliasis humana en Brasil bajo diferentes condiciones climáticas en el territorio nacional. Metodología: Se realizó una encuesta de casos de fascioliasis humana en Brasil utilizando las bases de datos Google Scholar, Lilacs y PubMed. Las variables climáticas como temperatura, precipitación, humedad y altitud se obtuvieron de la base de datos del Instituto Nacional de Meteorología (INMET). Resultados: Entre los años 1958 y 2022 se registraron sesenta y seis casos de fascioliasis humana en lugares con temperatura entre 22 °C a 33 °C, humedad entre 78% y 86%, precipitación entre 90 mm y 167 mm y una altitud de 16 a 935 metros sobre el nivel del mar. Conclusión: La capacidad de adaptación del parásito a diferentes condiciones climáticas se observa en Brasil y el número de casos de fascioliasis humana en el territorio nacional puede ser mayor debido al subregistro relacionado con la dificultad en el diagnóstico de la infección.
PALABRAS CLAVE: Fascioliasis; Fasciola Hepatica; Trematodo; Clima; Zoonosis Desatendida.

1. INTRODUCTION

Human fascioliasis is a plant-borne and water-borne infection caused by the trematodes *Fasciola hepatica* and *Fasciola gigantica*. It is one of the main neglected tropical diseases, and infections in humans occur via the ingestion of contaminated water and food (ASHRAFI et al., 2006). Metacercariae are the infective forms of the parasite, and freshwater snails of the genus *Lymnaea* are the main intermediate hosts of *Fasciola hepatica* (MAS-COMA, VALERO, BARGUES, 2022).

In the acute phase of infection, non-specific signs and symptoms such as fever, abdominal pain, gastrointestinal disturbances, urticaria, and respiratory symptoms are among the major symptoms observed (KAYA, BESTAS, CETIN, 2011; MARCOS, TERASHIMA, GOTUZZO, 2008); however, many cases are asymptomatic. In chronic infection, the individual can progress to complications such as liver abscess,cholelithiasis, cholecystitis (ARJONA et al., 1995; GORAL et al., 2011; KAYA, BESTAS, CETIN, 2011; KEISER et al., 2005; MARCOS, TERASHIMA, GOTUZZO, 2008).

The diagnosis of the infection in humans can be performed by a combination of a direct method, such as examination of eggs in the feces of the individual, or an indirect method such as serological tests that identify an IgG or IgM antibodies against the parasite (MAS-COMA, BARGUES, VALERO, 2014; VALERO et al., 2012). Imaging examinations such as computed tomography, magnetic resonance imaging, and abdominal ultrasonography are also used for diagnosis of chronic cases (DUSAK et al., 2012).

The treatment of human fascioliasis is with the drug triclabendazole, which was approved by the FDA in 2019. The initial dose is 10 mg/kg orally, and the dosage can be increased in case of treatment failure to two doses of 20 mg/kg with an interval of 12 – 24 hours; the efficacy of the drug corresponds to 90% after treatment (GANDHI et al., 2019; MARCOS, MACO, TERASHIMA, 2021).

The adaptation of the parasite to different climatic conditions allows a wide dispersion of *Fasciola hepatica* in the world. It has been described in 51 countries on 5 continents (FURST, KEISER, UTZINGER, 2012), and affects approximately 2.4 to 17 million people worldwide (MAS-COMA, VALERO, BARGUES, 2019). In South America, human fascioliasis is endemic in Peru, Chile, Argentina, Colombia, and Venezuela, and many human cases have also been reported in high altitude areas of the Bolivian region between Lake Titicaca and the valley of the city of La Paz (APT et al.,

1993; ARTIGAS et al., 2011; BARGUES et al., 2011a, 2011b; MERA y SIERRA et al., 2011; VALERO et al., 2012; VILLEGAS et al., 2012).

Considering that there are only few investigative studies on human fascioliasis in Brazil, the lack of knowledge about the disease by a large part of the population and by some health professionals, this study brings a review of all cases of human fascioliasis registered in Brazil, showing the locations of occurrence of the disease, the tests used for the diagnosis and the adverse climatic conditions of these localities, contributing scientifically with epidemiological information that can be of substantial help to other research studies on the disease.

2. METHODS

2.1 Bibliographic review of human fascioliasis cases in Brazil

The cases of human fascioliasis registered in Brazil were obtained through a bibliographic search carried out from May 2021 to February 2022 of the PubMed, Lilacs and Google Scholar databases, using the combined descriptors “human fascioliasis and Brazil”, “fascioliasis and Brazil” for the search The selection process of papers was carried out based on reading their titles, abstracts, and full text, following four phases for the selection: identification, selection, eligibility and inclusion.

2.2 Climate variables

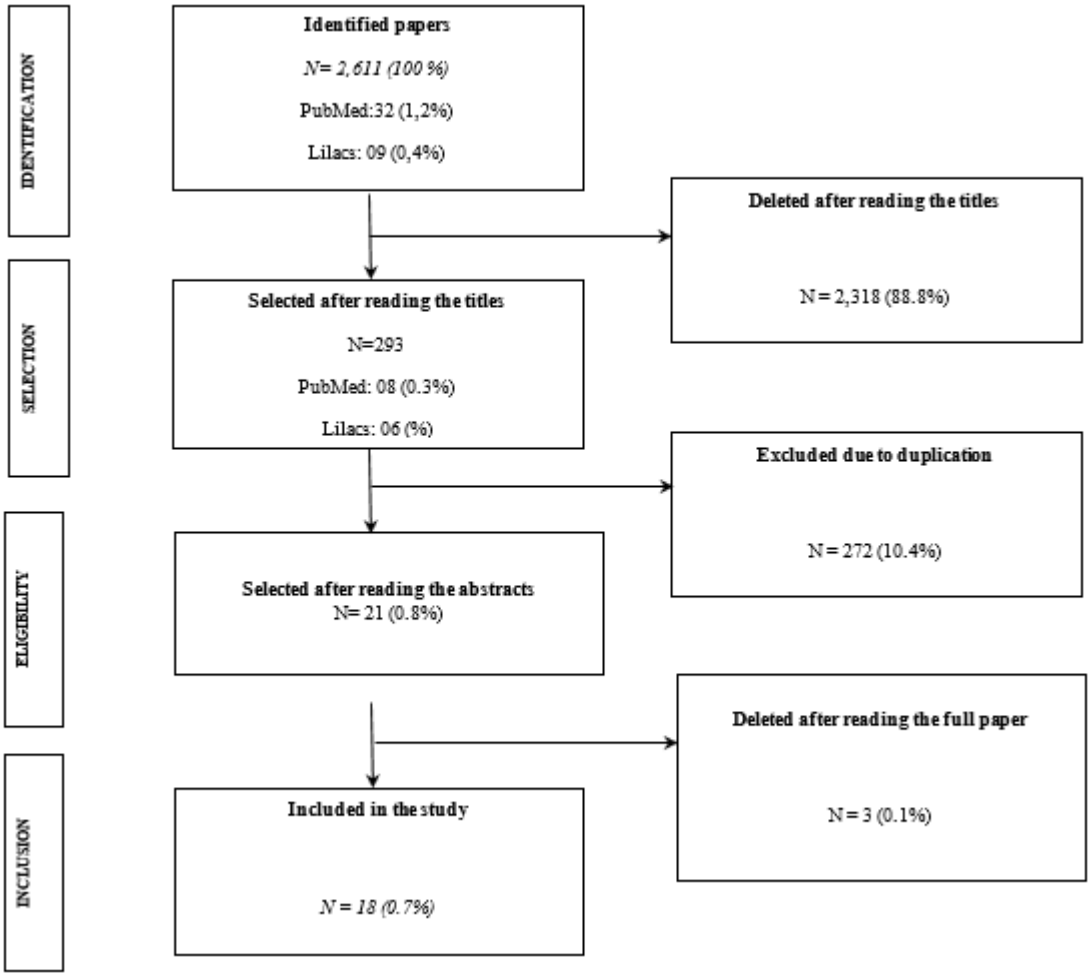
In this study, the following climatic variables were analyzed: precipitation, temperature, humidity and altitude of the locations where there was a report of human fascioliasis. The variables were obtained from the database of the National Institute of Meteorology (INMET), and an average of these variables was calculated for the years between 2000 to 2017, which is represented in a thematic map built in the ArcGis Program.

3. RESULTS

3.1 Spatial distribution of human fascioliasis cases

The initial search in the databases yielded a total of 2,611 publications, 32 from PubMed, 9 articles from Lilacs and 2,570 papers from Google Scholar. Out of this total, 2,318 were excluded after reading the title, which left 293 papers. Due to duplication 272 studies were excluded and, after reading the abstracts and the full text of the remaining 21 articles, 3 were excluded, leaving 18 articles that were used in the study (Figure 1).

Figure 1 - Flowchart of the selection process for inclusion of studies



In Brazil, 66 cases of human fascioliasis were recorded in 20 municipalities in 10 Brazilian states between the years 1958 to 2022. The cases were distributed in the states of Mato Grosso do Sul (2 cases), Rio Grande do Sul (1 case), Santa Catarina (1 case). case), Rio de Janeiro (4 cases), Bahia (9 cases), Ceará (1 case), São Paulo (8 cases), Amazonas (19 cases) and Paraná (20 cases) (Table 1).

Table 1 - Human fascioliasis cases reported from 1958 to 2022 in Brazil, including the city or region and the method of diagnosis.

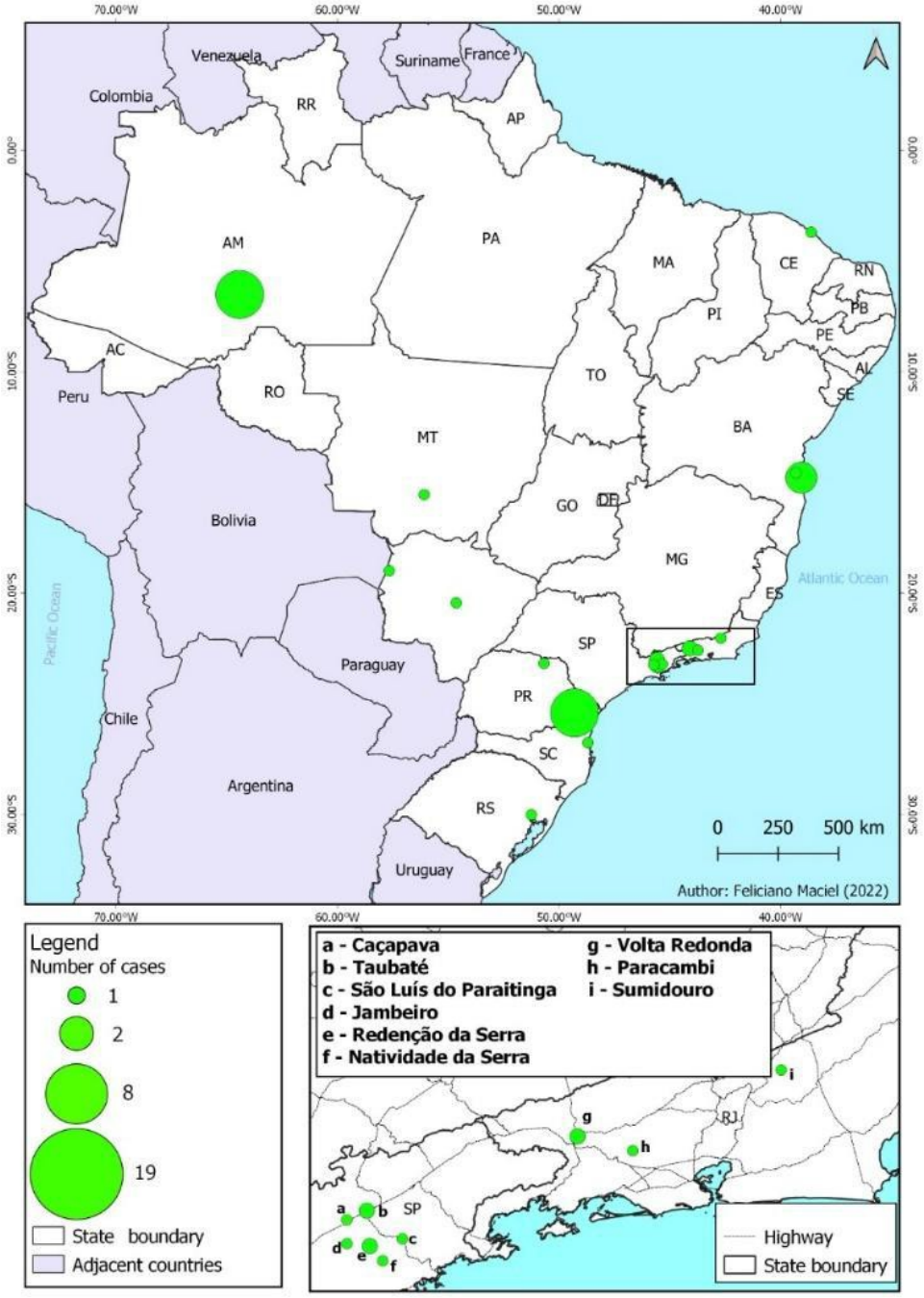
Author(s)	Year	City-State	Positive samples	Diagnostic method
Rey	1958	Campo Grande (MS)	1	Hoffman, Pons & Janer
Santos	1967	Uruçuca, Ilhéus (BA)	2	Hoffman, Pons & Janer
Santos & Vieira	1967	Taubaté, Redenção da Serra, São Luiz do Paraitinga, Natividade da Serra, Jambeiro (SP)	7	Hoffman, Pons & Janer and Faust & col. duodenal tube and intradermal reaction
		Cornélio Procópio (PR)		Hoffman, Pons & Janer
Corrêa & Fleury	1971	Caçapava (SP)	1	Fecal egg and parasite presence
Amato Neto & Silva	1977	Curitiba (PR)	1	Hoffman, Pons & Janer
Baranski et al.	1978	Curitiba (PR)	2	Ether sedimentation
Amaral & Busetti	1979	Curitiba (PR)	8	Fecal exam Fecal exam

Andrade Neto et al.	1999	Volta Redonda (RJ)	9	Endoscopic retrograde cholangiography
Pile et al.	2000	Cuiabá (MT)	2	
Mezzari et al.	2000		1	Hoffman, Pons & Janer and Kato-Katz
Igreja et al.	2004	Paracambi, Sumidouro (RJ)	2	Choledochoscopy
Coral et al.	2007	Canutama (AM)	1	Hoffman, Pons & Janer
Oliveira et al.	2007	Fortaleza (CE)	11	ELISA, Western Blot, Lutz
Almeida Filho et al	2017	Canutama (AM)	1	Ultrasound, ELISA
Maciel et al.	2018	Balneário Piçarra/SC	8	Hoffman, Pons & Janer
Pritsch et al	2019	Corumbá (MS)	1	Kato-Katz
Da Silva et al.	2019	Ilhéus (BA)	1	
Oliveira et al.	2020		7	

	Total	**66**

The highest number of cases was reported in the State of Paraná, where 20 cases of parasitosis were registered, and the lowest numbers were in the states of Rio Grande do Sul, Santa Catarina, and Ceará with one record each (Figure 2).

Figure 2 - Distribution of human fascioliasis cases in Brazil



3.2 Climatic variables in municipalities with a record of human fascioliasis

3.2.1 Precipitation variable

The average rainfall in the municipalities with a record of human fascioliasis ranged from 90 mm to 167 mm. The municipality of Canutama (AM) had the highest rainfall with 167 mm and the lowest record, with 90 mm, was in the municipalities of Caçapava and Jambeiro (SP) (Figure 3A).

3.2.2 Temperature variable

In the period from 2000 to 2017, the temperature averages in the 20 municipalities where there was a record of human fascioliasis ranged from 22 °C to 33 °C. The municipality of Canutama (AM) had the highest temperature record (33 °C) and the lowest (22 °C) was in the municipality of Balneário Piçarra (SC) (Figure 3B).

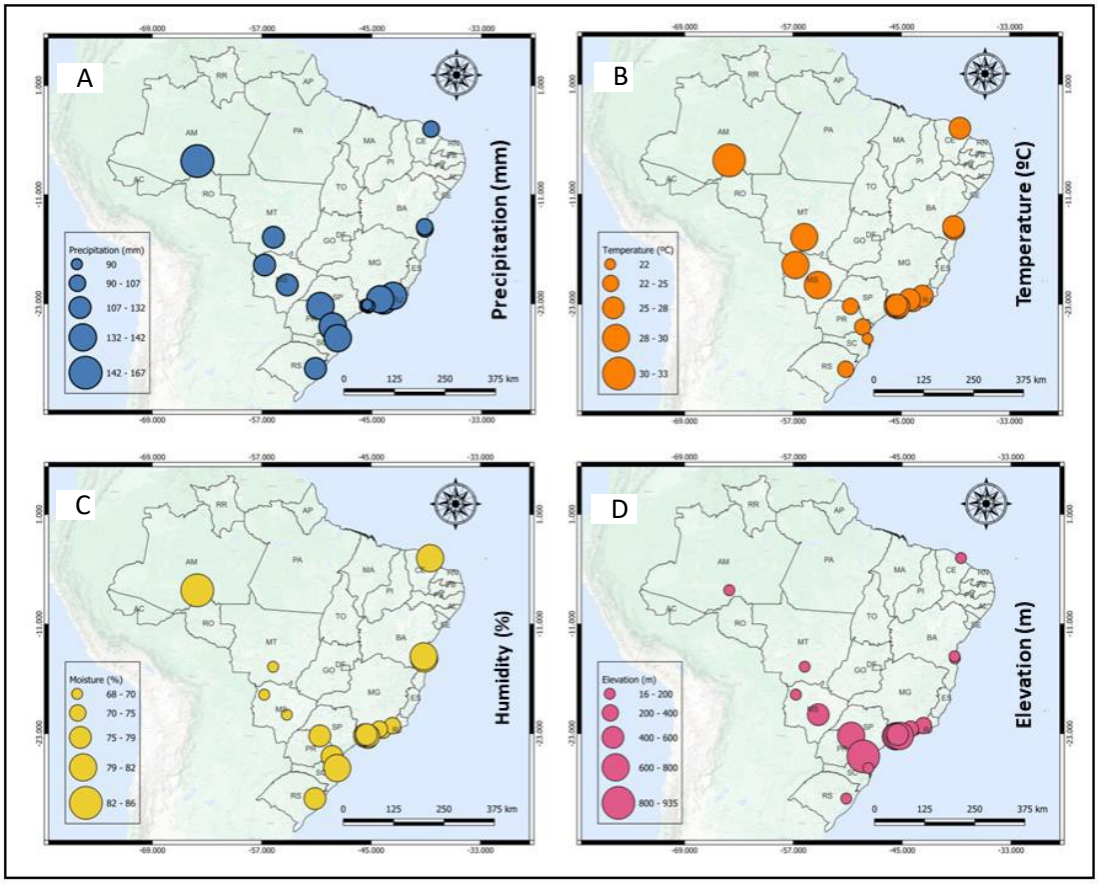
3.2.3 Humidity Variable

There were variations in humidity from 78% to 86%, with the highest record in the municipality of Canutama (AM) with 86%, and the lowest record in the municipalities of Natividade and Taubaté (SP) with 78% (Figure 3C).

3.2.4 Elevation variable

The municipality of Curitiba (PR) has the highest altitude at 935 meters above sea level and Fortaleza (CE) has the lowest altitude at 16 m (Figure 3D).

Figure 3 - Climatic variables in locations where cases of human fascioliasis were reported in Brazil



4. DISCUSSION

The process of global warming has caused constant changes to our climate, affects ecosystems and alters the dynamics of some infectious diseases (BARCELLOS et al., 2009), especially, diseases transmitted by water since the increase in water collections allows the dispersion of the hosts and the vectors. The dynamics of transmission and dispersion of human fascioliasis are susceptible to these climate changes since it is a zoonosis transmitted by food and also by water.

The cases of human fascioliasis recorded in Brazil were diagnosed using coprological, serological (ELISA and Western Blot) and imaging tests such as choledochoscopy and endoscopy (ALMEIDA FILHO et al., 2017; AMARAL, BUSSETTI, 1979; AMATO NETO, SILVA, 1977; BARANSKI et al., 1978; CORAL, MASTALIR, E., MASTALIR, F., 2007; CORRÊA, FLEURY, 1971; DA SILVA et al., 2019; IGREJA, BARRETO, SOARES, 2004; LUZ et al., 1999; MACIEL et al., 2018; MEZZARI et al., 2000; OLIVEIRA et al., 2007; OLIVEIRA et al., 2020; PILE et al., 2000; PRITSCH et al., 2019; REY, 1958; SANTOS, 1967; SANTOS, VIEIRA, 1967). Due to the difficulty involved in diagnosing parasitosis in humans, it is recommended to

combine different examination methods, such as coprological and serological exams (MAS-COMA, BARGUES, VALERO, 2014), and additional helpful non-invasive diagnostic techniques, including radiology, radioisotope scanning, ultrasound, computed tomography and magnetic resonance (DUSAK et al., 2012).

Cases of human fascioliasis are described in locations of high precipitation, temperature, humidity and at an altitude of 940 meters above sea level, as well as in areas of low precipitation, temperature, humidity and altitude of 18 meters. Brazil has adverse weather conditions in its northern, northeastern, southern, southeastern and central-western regions. In the Amazon region, there are only two well-defined seasons during the year, periods of sun and rain, while in the southern and southeastern states there are four seasons: spring, summer, autumn and winter (GRIMM, NATORI, 2006).

In the northern region of Brazil, the parasitosis is described in the municipality of Canutama, which is located in the south of the state of Amazonas and, coincidentally, borders the state of Mato Grosso, is also where cases of the parasitosis in cattle have been described (BENNEMA et al., 2014). The climatic conditions in this location are typically those of a tropical climate, in which high temperatures and high rainfall prevail throughout the year.

The description of a case in the state of Bahia in northeastern Brazil, where climatic conditions are very different from the Brazilian Amazon region, shows the possibility of the parasite's adaptation in a region with semi-arid areas with little precipitation, high temperatures and low humidity (MARENGO et al., 2011), compared to the state of Amazonas and with states in the central-western region of Brazil where higher levels of precipitation, temperature and humidity are recorded.

Dutra et al. (2010) mapped areas at risk of fasciolosis in cattle in the states of Paraná, Rio Grande do Sul and Santa Catarina in southern Brazil, which are areas with an average temperature of 19.5 °C, and an elevation of between 5 at 154 meters above sea level; however, in our study we describe cases of human fasciolosis in locations with average temperatures of between 22 °C to 33 °C and an elevation of 16 to 935 meters above sea level.

The transmission of fascioliasis is determined by climatic factors, such as temperature, precipitation and humidity (AFSHAN et al., 2014), as they are the determinants for the success of the population dynamics of the intermediate hosts that have flooded areas as their habitat, and these are usually formed in periods of greater

intensity of rain. In this study, precipitation ranged from 90 to 167 mm and humidity between 75% to 86%.

The occurrence of human fascioliasis in seven Brazilian states with different climatic conditions shows that the dispersion of the parasite to different locations in Brazil has been occuring gradually, thus confirming the adaptability of *Fasciola hepatica* and its intermediate hosts to climatic adversities (MAS-COMA, 2020), and favoring its expansion to unaffected areas.

The spread of human fascioliasis in Brazil may be related to the parasite's ability to adapt to different climatic conditions, and through the introduction of fascioliasis-infected animals from endemic areas into unaffected areas, as well as the dispersion and adaptation of their intermediate hosts to different areas of the national territory.

5. CONCLUSION

The number of cases of human fascioliasis in the national territory may be higher, considering the underreporting, the difficulty of diagnosis and the lack of knowledge about the infection by health professionals and the population. This study shows the spread of infection to areas previously considered free of the disease, regardless of their climatic factors, showing the need for further studies on screening, treatment and control of this parasitosis in human populations of Brazil.

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