Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/17080
DOI URL: http://dx.doi.org/10.21474/IJAR01/17080

RESEARCH ARTICLE

THE NEW INCREASE IN THE RATE OF CONTAMINATION AND DEATHS RESULTING FROM SPOTTED FEVER IN BRAZIL

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Manuscript Info

Manuscript History
Received: 11 April 2023
Final Accepted: 14 May 2023
Published: June 2023

Key words:-
Mortality, Rickettsia, Rocky Mountain Spotted Fever, Epidemiological Monitoring

Abstract

Rocky Mountain spotted fever is an infectious, acute febrile disease of variable severity. It can range from mild and atypical clinical forms to severe forms, with a high lethality rate. Rocky Mountain spotted fever is caused by a bacterium of the genus Rickettsia, transmitted by tick bites. In Brazil, two species of rickettsiae are associated with clinical conditions of Spotted Fever. Rickettsia rickettsii, which leads to Brazilian Spotted Fever (BSF), considered a serious disease, registered in the north of the state of Paraná and in the states of the Southeast Region. Rickettsia parkeri, which has been recorded in environments of the Atlantic Forest (Rio Grande do Sul, Santa Catarina, Bahia and Ceará), producing less severe clinical conditions.The objective of this article wasto describe through a literature review, Rocky Mountain spotted fever in Brazil, forms of transmission, treatment, mortality and clinical manifestations.In Brazil, the main vectors are ticks of the genus Amblyomma, such as A. sculptum (= A. cajennense) known as the star tick, A. aureolatum and A. ovale. However, potentially, any species of tick can harbor the bacteria that cause Rocky Mountain Spotted Fever, such as the dog tick.

Introduction:-

Spotted Fever was identified for the first time in the State of Idaho, in the United States, at the end of the 19th century (Bajwa et.al, 2022).

Its name was due to its great incidence in the American states cut by the chain of the Rocky Mountains. In 1906, the etiological agent, Rickettsia rickettsii (rickettsia) was described by Howard Taylor Ricketts, who also identified the tick as the main transmission vector (Bajwa et.al, 2022).

Rocky Mountain spotted fever is very similar to typhus. Because of this similarity, Ricketts was invited to collaborate on research during a typhus epidemic in Mexico. Days after isolating and identifying the microorganism that caused the disease, he became infected and died of typhus in 1910 (Faccini-Martínez et.al, 2018).

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In Brazil, spotted fever is also known as tick-borne typhus, petechial fever, or Brazilian spotted fever. It was recognized for the first time in Brazil, in 1929, in São Paulo. Soon after, it was described in Minas Gerais and Rio de Janeiro. The gram-negative bacterium Rickettsia rickettsii, which causes Rocky Mountain spotted fever, is obligate intracellular and resides in the cytoplasm of the host, both the vertebrate and the invertebrate vector that transmits it (Moraes-Filho, J., 2017).

In Brazil, most cases of Rocky Mountain spotted fever are concentrated in the Southeast Region, with scattered cases in other Brazilian states, especially in southern Brazil (Cardoso et.al, 2006;Moraes-Filho, J., 2017).

This higher incidence coincides with the presence of main vector and reservoir — the star tick — Amblyommacajennense. They are still associated with transmission of Rocky Mountain spotted fever to Amblyommaaureolatum and Amblyommadubitatum. (Nogueira et.al, 2022).

The sazonality of disease incidence is important and is related to increased tick activity. The promoting greater contact with humans, taking place from June to October.

The tick is located limestone in pastures and lawns, preferably in places far from the sun, well shaded and close to we go to rivers and lakes(Moraes-Filho, J., 2017).

According to recent data from the Ministry of Brazilian Health (2022), the country recorded an increase in the number of cases compared to the previous year, with eight deaths already confirmed.This reality is alarming and requires attention from health professionals, students and the general public(Nogueira et.al, 2022).

Although in Brazil the number of confirmed cases of Rocky Mountain spotted fever has been declining since 2015, the mortality rate (20 to 30%) is still very high when compared to other countries. This high mortality rate is closely related to the difficulty in making the diagnosis and establishing appropriate therapy (Nogueira et.al, 2022).

Objectives:-

To describe through a literature review, Rocky Mountain spotted fever in Brazil, forms of transmission, treatment, mortality and clinical manifestations.

Material And Methods:-

This study is descriptive in nature, and used a literature review of published studies on Rocky Mountain spotted fever as a methodology.

Portals were used; The National Library of Medicine (NCBI) and the Virtual Health Library (BVS), in which the following research sources were accessed: Cochrane Library, IBECS, Scientific Electronic Library Online (SciELO), PubMed.

All total of 26 articles were considered for this review study. The type of study was based on a descriptive method. After reviewing the literature and searching for relevant works consistent with the theme proposed in this article, textual, thematic and interpretative analysis were carried out.

TransmissionofRickettsiae

The transmission of rickettsiae occurs through the bite of the tick in any of its stages (larvae, nymph and adult). For the tick to transmit the disease, it is necessary for it to adhere to the skin, feeding, for a period of 6 to 10 hours. When pricking, and after feedingment, the tick transmits the microorganism by through your salivary glands. It is important to note than the bites of larvae and nymphs, because they are least painful, are the ones most likely to ability to transmit the microorganism, because the human beinghand does not notice the bite and allows the streaming (Otsuki et.al, 2023).

The adult sting, as it is very painful, rigid, is readily perceived, and the carraped in time to not transmit the disease. Other form of contagion occurs by crushing the tickduck when it is removed, releasing its gas knit (Lu, M. et.al, 2022).

Mortality and pathogenesis

The mortality rate is clearly related to nothing to early diagnosis and rapid installation of appropriate therapy.In cases where therapy is initiated in the first 3 days of illness, the death rate rate is around 2% in children and 9% in elderly (> 65 years).Patients with deficiency of glucose-6-phosphate dehydrogenase also have higher mortality rates, probably in lower activity of the immune system (Castillo- Contreras et.al, 2022).

From the bite of the infected tick, the Rickettsia spreads throughout the body via lymphatic vessels, cells and small blood vessels, reaching the skin, cervix,rebro, lungs, heart, liver, spleen, pancreas and tract gastrointestinal. In all affected tissues, the Rickettsia invades the vascular endothelium, where it replicates to target smooth muscle cells. the rickettsiae, bind to cholesterol-containing receptors,to endothelial cells through specific proteins, (ompA and ompB) and interacting with a receivercell (Ku70 protein kinase) (Bourchookarn et.al, 2022).

The penetration intohost cells occurs by induced phagocytosis.Later, with the rupture of the phagosome, themicroorganism reaches the cytoplasm, where it multipliesplica by binary fission with replication time ofapproximately 10 minutes, with the penetrationendothelial cells, an inflammatory response occursacute phase, mediated by the production of cytocy-such as TNF-alpha and IFN-gamma, resulting in increasedvascular permeability, hypovolemia andconsequent hypoalbuminemia (Otsuki et.al, 2023).

At all sites of infection, there is aexcessive consumption of platelets, which leads to thrombosisbocytopenia in about 40% of infected patients (Chao et.al, 2022).

With the extensive endothelial injury, aprocoagulant state, with activation of the coaggregation, thrombin release, increased aggregationplatelet aggregation and increase in antifibrinolytic factors(Chao et.al, 2022).

The condition worsens with thrombosis ofsmall vessels of the heart, kidneys, lungs and brain.It also occurs, due to the blockage of smallvessels, tissue necrosis and cerebral ischemia, mainlymind of the mesencephalon and region of the nuclei (23).

The possible mechanism for endothelial cell injurycaused by rickettsia appears to be ATP depletion,which would lead to a decrease in the functioning of thesodium pump in the cell membrane(Otsuki et.al, 2023).

In addition, endothelial cells are activated after insertioninfection, with concomitant production of cytokines thatstimulate the acute phase response, with activation ofphagocytes and NK cells. CD8 lymphocytes and NK cellsare found in the perivascular infiltrate, possiblymind to control the infection, since bothplay an important role in the immune response againstintracellular microorganisms (Chao et.al, 2022).

The inflammatory responseand immunological mediated by increased cytocyat Th1 and Th2 seems to be important in the process ofdisease containment(Chao et.al, 2022).

The incubation period for Rocky Mountain spotted fever canvary from 2 to 14 days, with an average of 7 days until thesymptoms, and is related to the sizeof the inoculum at the time of infection (Bishop et.al, 2022).

The maculopapular rash, the main signto define the diagnosis, appears in few patients (Bourchookarn et.al, 2022).

On the 1st day of illness, showing up in about 49%of patients up to the 3rd day and in 91% of patients up to the 5thday. Delay in the appearance of macular rashdetermines delay in diagnosis and worsening prognosis (Chao et.al, 2022).

Due to the difficulty in using the appropriate treatmentsquare. The lack of this signal makes the diagnosis very difficult (Otsuki et.al, 2023).

The clinical diagnosis, reaching 9 to 12% ofinfected, especially the elderly and people withblack skin. The macules have a pink, burgundy appearance (Condit et.al, 2022).

The poorly defined, with 2 to 6 mm in diameter; have heat usually around the wrists and ankles,also start in the chest region. The stains,at first, they disappear when pressed, but thiseffect disappears with time and the darkening of thecoloring (Di Cataldo et.al, 2022).

The appearance of the rash on the palmsbut of the hands and soles of the feet, despite occurring withmuch variation (40 to 80% of patients), it is considereda very characteristic sign of Rocky Mountain spotted fever. The netissuecrosis and gangrene, especially of the fingers andears, occurs in up to 4% of patients(Condit et.al, 2022).

Clinical manifestations

Initial symptoms are nonspecific, with thepatient presenting high fever, around 39.5ºC,speech, myalgias, general malaise and hyperemiaof the conjunctivae. The gastrointestinal symptoms appearhundred in a significant number of patients (Dowling et.al, 2022).

The symptomsincludes vomiting, diarrhea and abdominal pain, and maybe confused with acute abdomen. Hepatoesplenomegaly may be present in up to 33% ofpatients (Zhang et.al, 2023).

With the lack of treatment and the progression offramework, there may be compromise of the systemcentral nervous system, characterized by severe encephalitis,determining mental confusion (28% of patients),delusions (20 to 26%), ataxia (5 to 18%), seizures (8%)and eat (9 to 10%). The presence of the microorganism in theblood vessels of the meninges and brain leads topresence of leukocytes in CSF — 10 to 100 per Ml and increased protein in about 35% of patients (Pascucci et.al ,2023).

With increased vascular permeability,dehydration with hypovolemia, insufficiencypre-renal and great protein loss, explaining the fourclusters of generalized edema. Renal involvement isindicative of a serious prognosis (Philip et.al, 1978; Pascucci et.al, 2023).

Pulmonary involvement is evidenced by thepresence of cough and radiological findings, such as infiltrationalveolar tract and interstitial pneumonia. The pulmonary edemaMonar with decreased respiratory function canrequire respiratory support and oxygen therapy (Lin, B., Ta, Y., &Hao, L. 2022).

Trataments

Only two groups of antibiotics have proven clinical efficacy, chloramphenicol and tetracyclines. Until recently, tetracyclines were reserved for adult patients due to dental and bone alterations in children. Recently, however, the American Academy of Pediatrics and several authors have recommended the use of doxycycline in children as well. In more severe cases, the lack of experience with an injectable tetracycline in Brazil makes one opt for injectable chloramphenicol. As prompt diagnosis and adequate choice of drug are determining factors of a positive prognosis, all health professionals should be better prepared to recognize and treat Rocky Mountain spotted fever(Dowling et.al, 2022).

Beta-lactam agents and aminoglycosides do notshow any activity against rickettsia. To thesulpha drugs are absolutely contraindicated, as they actas a substrate and nutrition factor for the microorganism, further facilitating its replication, with consubsequent worsening of the clinical condition (Zhu et.al, 2022).

The eschoose between chloramphenicol and tetracycline (doxycycline)relates to the severity of the disease.

In more severe cases, due to the absence ofin Brazil of a tetracycline for intravenous use,chloramphenicol is recommended. In adults, chloramphenicol should be used at a dose of 50 to 75 mg/kg/day,6 in 6 hours. In general, 1 g of chloramphenicol is usedIV every 6 hours until there is an improvementon the general condition of the patient, substituting therapyparenterally orally, at a dose of 500 mg every 6hours (Pascucci et.al ,2023).

The treatment time is generally 7 days, or2 days of antibiotics can be used as a parametertherapy after remission of the febrile condition. In childrensevere cases, intravenous chloramphenicol should be used indoses of 50 to 100 mg/kg/day, every 6 hours, untilrecovery of consciousness and improvement of the conditiongeneral practitioner, never exceeding 2 g per day (Dowling et.al, 2022).

In patients with less severe conditions, the preference is for doxycycline, used orally. AlSome studies have demonstrated, clinically, theirgreater effectiveness in the treatment of Rocky Mountain spotted feverwhen compared to chloramphenicol (Behera et.al, 2023).

Studiesin vitro comparing the susceptibility of Rickettsiarickettsii to the two drugs also demonstrate theduration of doxycycline (Behera et.al, 2023).

In adults, doxycycline should be usedin twice daily doses of 100 mg for 7 days or for2 more days after the remission of the febrile condition. Inchildren, although several authors do not recommend theuse of no tetracycline in children under 9 years of age infunction of the brownish pigmentation effect, recently the American Academy of Pediatricsrecommended the use of doxycycline, regardless ofaging, due to its greater effectiveness (Elelu et.al, 2022).

Other works have supported this proposition.The dose of doxycycline used inchildren weighing less than 45 kg is 2.2 mg/kg every 12hours. Children with greater weight should use the doseof the adult (Dowling et.al, 2022).

The greater risk of stains when there isemployment in pregnant women and newborns occurs in thefirst dentition, although there is a risk of pigmentationpermanent when used between 2 months and 5years old (Jakimovski et.al, 2022).

The involvement of tooth enamelrisk from the use of tetracyclines is dose-dependent, and the treatmentTreatment of rickettsial diseases involves a short periodof doxycycline use (Elelu et.al, 2022).

Regarding pregnant women, although some authors recommend the use of doxycycline in this population (Elelu et.al, 2022).

The risk of alterations in the dental enamel is great,preference should be given to intravenous chloramphenicolnosally or orally, depending on the severity of the disease, andit is important to remember that pregnant women should avoiduse of chloramphenicol 30 days before delivery due togray syndrome in neonates. In that case, recommenddoxycycline is recommended (Fiol et.al, 2010; Elelu et.al, 2022).

Brazilian Spotted Fever and other rickettsial diseases

In Brazil, the most important ticks in the transmission of the bacteria are of the genus Amblyomma, according to Labruna et al., (2011): Amblyommaaureolatum; Amblyommadubitatum; Amblyommaovale;Amblyommasculptum (Amblyommacajennensesensulato) (Dantas-Torres et.al, 2022).

Equids, rodents such as the capybara (Hydrochaerishydrochaeris), and marsupials such as the opossum (Didelphis sp) play an important role in the spotted fever transmission cycle and there are recent studies on the involvement of these animals as amplifiers of rickettsiae, as well as transporters of ticks potentially infected (Dantas-Torres et.al, 2022)

The FIGURE 1 shows the Distribution of Brazilian municipalities and Federated Units with trained professionals for the proposed structuring of the National Environmental Surveillance Network for Spotted Fever and Other Rickettsioses in Brazil.

Figure 1:- Distribution of Brazilian municipalities and Federated Units with trained professionals for the proposed structuring of the National Environmental Surveillance Network for Spotted Fever and Other Rickettsioses in Brazil.

20 years ago, Rocky Mountain spotted fever was included in the compulsory notification list in Brazil, that is, the disease must be mandatorily communicated to the public health authorities. Due to the date, the Ministry of Health released an Epidemiological Bulletin, with the objective of describing the profile of the disease and presenting historical milestones since its discovery in the country until the present day. The publication took place last Monday (20), during the webinar "Surveillance of Spotted Fever in Brazil "(Dantas-Torres et.al, 2022; de Souza et.al, 2023).

The transmission of FMB is associated with ticks of the Amblyomma genus, and the most important species in the transmission of the disease are A. sculptum (formerly A. cajennense) and A. aureolatum. The disease is characterized by fever, myalgia and severe headache, rash, edema in the hands and feet, and in some cases it is generalized. The disease causes sepsis with pulmonary involvement, which may lead to acute respiratory failure, kidney problems, such as acute renal failure, hemorrhagic diathesis, neurological lesions with meningitis, encephalitis and jaundice (de Souza et.al, 2023)

Clinical cases that evolve to death due to late diagnosis and treatment usually occur between the 5th and 15th days after the onset of symptoms. The diagnosis of the disease is made using the indirect immunofluorescence reaction (IFAT), polymerase chain reaction (PCR) and isolation in cell culture (Moraes-Filho, J., 2017).

Every suspected case requires immediate notification, registered in the Notifiable Diseases Information System (SINAN), by filling out the Spotted Fever Investigation Form (Nogueira et.al, 2022).

The FIGURE 2 shows thenotified and confirmed cases of Rocky Mountain spotted fever, according to the municipality of notification and infection, and RGFM infections in vectors collected in silent areas of Brazil, 2021 to 2022.

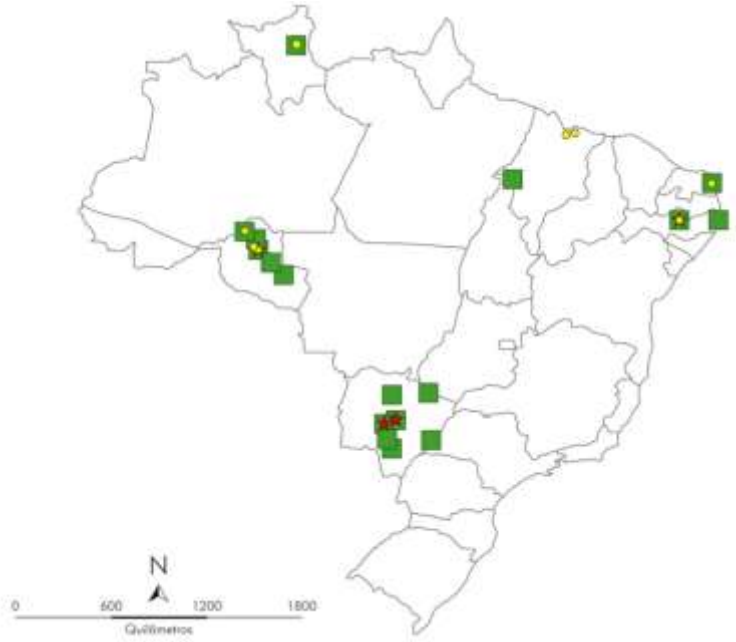

Figure 2:-Thenotified and confirmed cases of Rocky Mountain spotted fever, according to the municipality of notification and infection, and RGFM infections in vectors collected in silent areas of Brazil, 2021 to 2022.

After the onset of clinical manifestations, treatment should be started early, interrupting the administration two or three days after the disappearance of the fever. Surveillance and control measures should focus on educational actions and disseminate the disease to the population and health professionals, passing on knowledge about its existence, about preventive measures and about the importance of sending ticks collected from patients or found in the environment to identify them (Dantas-Torres et.al, 2022; de Souza et.al, 2023).

Brazilian Spotted Fever and other rickettsial diseases have been reported in rural and urban areas in Brazil. The highest concentration of cases is seen in the Southeast and South regions, where it generally occurs sporadically. It affects the economically active population (20-49 years old), mainly men, who reported exposure to ticks, domestic and/or wild animals or frequented forest, river or waterfall environments (Nogueira et.al, 2022).

According to the document, from 2007 to 2021, 36,497 cases of Rocky Mountain spotted fever were reported in Brazil, of which 7% were confirmed, in an average of 170 per year in this period. Of the 2,545 confirmed cases, 2,538 reported situations related to risk exposure and, of these, 68.5% frequented a forest environment (Nogueira et.al, 2022).

Of the confirmed cases, 70.7% were male, with a greater proportion in the 35-49 age group. As for risk exposure to animals, 74.7% reported having been exposed to ticks. Coming in second place, exposure to dogs and cats, with 41% of cases (Nogueira et.al, 2022).

Final Considerations

From the results presented in this study, it is possible to verify that the data available in the SINAN database about FM, although sufficient to carry out an epidemiological analysis of the disease, still deserve attention in terms of the completeness of the filling. With the data presented here, it was possible to conclude that FM is more frequent in the South and Southeast regions, and occurs with higher lethality in the Southeast region, where it affects economically active populations and the vast majority of patients require hospitalization. The disease is registered mainly from July to December, more frequently in October, and the infections occur mainly in the rural zone in people who frequent forests, forests, rivers or waterfalls, who have been exposed to ticks. In view of this, it is necessary to improve the filling in of notification and investigation forms by the Municipalities, through actions to raise awareness about the importance of information for decision-making to control spotted fever. Allowing greater agility in identifying cases, diagnosing the disease and implementing measures of prediction, prevention, control and

strengthening of Epidemiological Surveillance services in the States, collaborating to improve their health indicators.

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