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Original

Search for Hantavirus and Arenavirus in rodents from Villavicencio, Colombia

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ABSTRACT

Objective. To search Hantavirus and Arenavirus in small rodents and establish their spatial distribution in disturbed ecosystems in the municipality of Villavicencio, Meta, Colombia. **Materials and method.** A descriptive cross-sectional study was carried out from October 2018 to October 2019 in periurban and rural areas of the municipality of Villavicencio. Rodents were captured using Sherman-type traps and molecular detection of Hantavirus and Arenavirus was carried out by Polymerase chain Reaction technique. **Results.** A total of 50 rodents were captured belonged to 3 families and six species, the *Muridae* (76%) with the highest number of captured individuals, *Cricetidae* (22%) and *Echimydae* (2%). All samples were negative for the molecular markers of Hantavirus and Arenavirus. **Conclusions.** The study of mammalian hosts, particularly small rodents contribute to monitor diseases transmitted by these small mammals that act as reservoirs.

Keywords: Rodents; Hantavirus; Arenavirus; Zoonotic diseases (*Sources: Mesh, ICYT*).

RESUMEN

Objetivo. Realizar una búsqueda de Hantavirus y Arenavirus en pequeños roedores y establecer su distribución espacial en diferentes ecosistemas del municipio de Villavicencio, departamento del Meta, Colombia. **Materiales y método.** Se realizó un estudio descriptivo de corte transversal, entre octubre de 2018 octubre de 2019 en zonas periurbanas y rurales del municipio de Villavicencio. Se capturaron roedores empleando trampas tipo Sherman. La detección molecular de Hantavirus se llevó a cabo usando cebadores forward SAHN-S y reverse SAHN-C y para Arenavirus cebadores forward GP878+ y reverse GP1126. **Resultados**. Un total de 50 roedores fueron capturados, el éxito de captura fue del 1.7%. Los roedores capturados pertenecían a 3 familias y 6 especies, las familias más frecuentes fueron *Muridae* (76%) *Cricetidae* (22%) y *Echimydae* (2%). Todas las muestras resultaron negativas para Hantavirus y Arenavirus. **Conclusión.** El estudio de pequeños roedores contribuye con la vigilancia de enfermedades transmitidas por estos mamíferos que actúan como reservorios.

Palabras clave: Roedores; Hantavirus; Arenavirus; Enfermedades zoonóticas (*Fuentes: Mesh, ICYT*).

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INTRODUCTION

Rodents are the most diverse and broadest group among mammals (1); they play an essential role in the ecology of tropical habitats as seed dispersers and controllers of some insect populations. Rodents help pollination and are part of the food chain of snakes, mammals, and some birds (2,3). Due to the high number of litters and offspring, they play a role as indicators of disturbed ecosystems and generate problems when trying to control them. They have a broad spectrum of busy ecological niches due to dietary diversity, and their ability to adapt. As a result, rodents are present in most of the planet's intervened ecosystems (4,6).

Only 5% of rodents are considered pests because their habit of gnawing causes economic losses and damage to crops, as well as the transmission of zoonotic diseases such as leptospirosis, salmonellosis, Hantavirus, and American trypanosomiasis, among others (4,7), which represent a significant public health problem due to the close relationship between humans and companion or wild animals (8).

Many species of wild rodents have no contact with man or domestic animals. However, they may act as reservoirs of infectious agents in endemic foci for extended periods (4,7). When commensal rodents in rural areas come into contact with wild species, they allow infectious organisms to be transmitted to them, directly or indirectly transmitting these infectious agents to man and other animals (9).

In Colombia, Arenavirus and Hantavirus have been reported in different areas of the territory. However, these viruses are not notifiable diseases and therefore are not included in the country's febrile syndromic diagnoses of clinical and hospital centers. However, countries such as Argentina and Chile consider these disease reports mandatory due to increased cases during the summer season (10,11,12).

The department of Meta, due to its geographical location, diversity of vectors, forced relocation, and disorderly urbanization of the municipal capitals, meets all the conditions for the development and persistence of diseases transmitted by rodents and other vectors (13). The role and importance of small wild, domestic and peridomestic rodents in the ecology of infectious diseases have been neglected, despite recent interest in animals as a source of emerging diseases in humans(1,14,15).

Bearing in mind that there are no reports on Hantavirus and Arenavirus in small rodents in the Meta department. The objective of the present study was to detect Hantavirus and arenaviruses and the spatial distribution of rodents in the ecosystems of the municipality of Villavicencio.

MATERIALS AND METHODS

Type and area of study. A descriptive cross-sectional study was conducted between October 2018 and October 2019 in peri-urban and rural areas of the municipality of Villavicencio, Meta, Colombia (04° 09 N-73° 38 W), at an altitude of 467 meters above sea level and an average temperature of 30°C. The municipality is located in the foothills of the eastern Andes mountain range, between the Ocoa and Negro rivers and numerous minor affluents. Its habitat is characterized by the incredible biodiversity that constitutes significant biological reserves for many mammals (13).

Capture of specimens. Samplings were carried out in 7 villages using 60 Sherman-type traps of live capture (8 x 9 x 23 cm; Sherman Traps, Inc., Tallahassee, FL). The traps were placed strategically according to the accumulation of garbage, food storage sites, or cultivated areas. The traps remained active for seven days overnight. Traps were checked early the next day. The bait was a mixture of flake oatmeal with banana and peanut butter. Once the traps were checked, the specimens found were transferred and processed at a field station, conditioned for that purpose. Pregnant females were released. The preparation and euthanization of the animals were carried out following the biosecurity protocols suggested by the Centers for Disease Control and Prevention (CDC) (16).

Biological sample collection. The rodents were anesthetized with 0.1ml of 10% ketamine hydrochloride according to their weight and euthanized by cervical dislocation. Subsequently, morphometric parameters such as weight, measurement of the right hind leg, right ear, body length, tail, total length, sex, and reproductive status were recorded, and pregnant females were released (16). The extracted organs were placed in tubes in a solution of RNAlater™ as duplicates and subsequently preserved in liquid nitrogen. The rodent species were identified with standard taxonomic keys (3). The collections were sent to the Instituto de Investigaciones Biológicas de Trópico (IIBT) of the University of Córdoba.

RNA extraction. The RNA was extracted directly from lung tissue using ThermoFisher Scientific's commercial GeneJET Purification Kit (K0732), following the manufacturer's recommendations. The purified RNA was preserved at -80ºC until use. The concentration and purity of the DNA samples was quantified with a NanoDrop™ 2000 spectrophotometer with optical densities of 230, 260, and 280 nm once the reverse transcription (RT-PCR) was performed.

Hantavirus and Arenavirus detection. A polymerase chain reaction with reverse transcriptase was performed to obtain cDNA using the enzyme RevertAid Reverse Transcriptase 10,000 U from ThermoFisher Scientific™ and random hexamers (Random primers Promega C118A) in samples of RNA from lung tissue. The detection of Hantavirus-Orthohantavirus and Arenavirus-Mammarenavirus the forward SAHN-S (GATGAATCATCCTTGAACCTTAT) and reverse SAHN-C (CAAAACCAGTTGATCCAACAGGG) primers were used for Hantavirus (17). For Arenavirus primers forward GP878+ (GAYATGCCWGGIGGITAYTGT) and reverse GP1126- (TACCAAAAYTTTTTGTGTARTTRCAATA) were used (18). The mixture was prepared with 2.5 μL of PCR buffer (10X: 20 mM Tris-HCl (pH 8.0), 1 mM DTT, 0.1 mM EDTA, 100 mM KCl), 0.75 μL of $MgCl_2$ (50mM), 0.5 μL of dNTP's (10 mM), 1.25 μL of each primer (10 μM), 0.25 μL of Taq Polymerase Recombinant (Invitrogen), 13.5 μL of molecular grade water and 5 μL of cDNA product of reverse transcriptase, with a final reaction of 25 μL. The mixture was put into a ProFlexTM PCR System (Applied Biosystems) thermocycler at 35 cycles with the following temperatures: 94°C for 45 s, 60°C for 30 s, and 72°C for 30 s. Finally, the mixture was kept for 5 minutes at 72°C. Although there were no positive controls, the PCR adhered to the standardization protocol proposed by Morelis et al. (17) for Hantavirus to amplify a highly conserved region of the N segment of the Genome of South-American Orthohantaviruses with an amplification product of 264 base pairs (bp). The protocol described by Delgado et al. (18) for Arenavirus was followed, which amplifies a highly conserved glycoprotein of the S segment of the genome with a product of 295 base pairs (bp).

Data Analysis. Descriptive analysis of absolute and relative frequencies, central tendency measures, and distribution of morphometric data was done using InfoStat (19). For spatial distribution analysis and proportions of the identified rodents, the free version of QGIS 3.12 was used.

Ethical considerations. The Ethics Committee approved all the procedures carried out in this Cooperative University of Colombia project under the ethical concept No 029-2017. The permission of the National Authority of Environmental Licenses (ANLA) was granted to the University of Córdoba within the framework of collection of biological samples resolution 0914, August 4, 2017. In addition, for the present study, the ethical principles of animal experimentation enunciated by ICLAS, the International Council for Laboratory Animal Science, were recognized (20).

RESULTS

A total of 50 rodents were captured, with a capture success of 1.7%, distributed in 10 geographical areas of the municipality of Villavicencio (Table 1).

Table 1. Geographical areas and number of rodents captured in the municipality of Villavicencio, Meta.

Zones	Geographical location	N. of captures (n=50)	%
Buenavista	4.173205556 -73.680844445	1	2
Apiay	4.10583 -73.550643	3	6
El Cocuy	4.039963889 -73.601850000	1	2
Caños negros punto 1	4.119747222 -73.517511111	2	72
Caños negros punto 2	4.116933333 -73.516700000	4	
Caños negros punto 3	4.128277778 -73.528175000	11	
Caños negros punto 4	4.131419445 -73.548166667	19	
La llanerita	4.101050000 -73.487066667	6	12
Santander	4.099394444 -73.440913889	1	2
Santa Rosa	4.020277778 -73.488888889	2	4

52% (26/50) of the captured rodents were males, and 48% (24/50) were females. Rodents were categorized according to their age as young (52%, 26/50) and adults (48%, 24/50). These were distributed according to the capture area. The highest frequency was found in the peri-domiciliary area with 58% (29/50), followed by the area denominated as wild with 38% (19/50) and to a lesser extent in home areas with 4% (2/50) (Table 2).

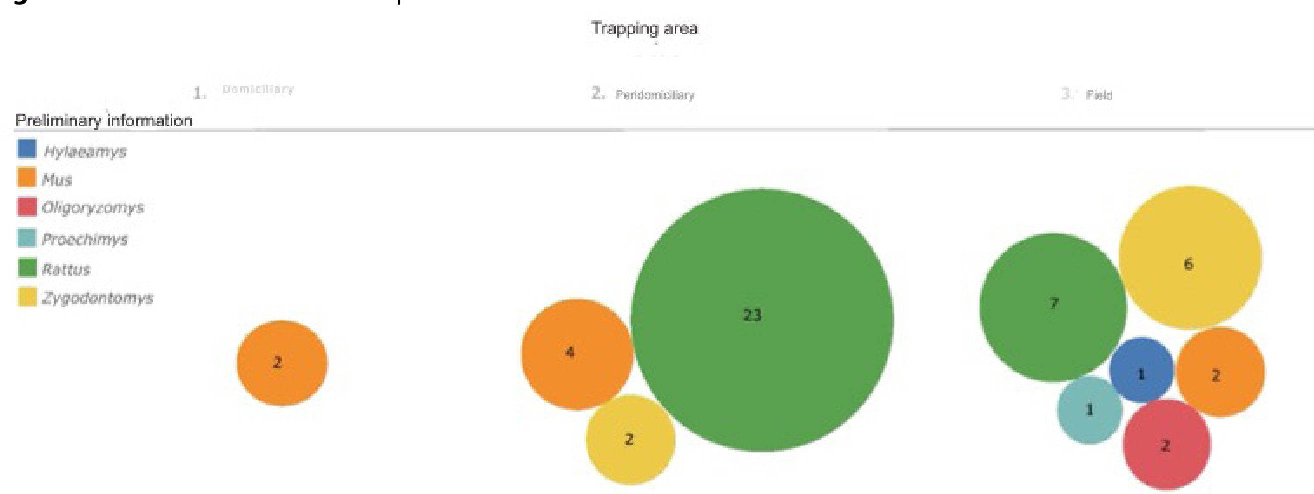
Table 2. Characterization of the captured rodents.

Sex	Frequency	%
Male	26	52
Female	24	48
Age category		
Young	26	52
Adult	24	48
Capture area		
1. Domiciliary	2	4
2. Peri-domiciliary	29	58
3. Field	19	38

In the peri-domiciliary áreas, 79.3% (23/29) of the captured rodents were *Rattus rattus*, 13.7% (4/29) *Mus musculus*, *Zygodontomys brevicauda* was found in a smaller proportion with 6.9% (2/29). In rural areas, 36.8% (7/19) belonged to *Rattus rattus* species, followed by *Zygodontomys brevicauda* with 31.6% (6/19), and less frequently *Oligorizomys sp* and *Mus musculus* with 10.5% (2/19) each and *Hylaeamy sp* and *Proechimys oconnelli* with 5.3% (1/19) each (Figure 1).

The 50 individuals were identified according to morphometric data (Figure 2). They were grouped into three families and six species. The family *Muridae* (76%, 38/50) was the one with the highest frequency of individuals captured, followed by the family *Cricetidae* with 22% (11/50) and, to a lesser extent, the family *Echimydae* with 2% (1/50). The most frequently caught specimens were *Rattus rattus* (60%), *Mus musculus* (16%), and *Zygodontomys brevicauda* (16%). *Oligoryzomys sp*, *Hylaeamys* (formerly *Oryzomys*), and *Proechimys oconnelli* (Table 3) were captured less frequently.

Figure 1. Distribution of rodent species in different áreas.



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All the samples were negative for the molecular markers of Hantavirus and Arenavirus.

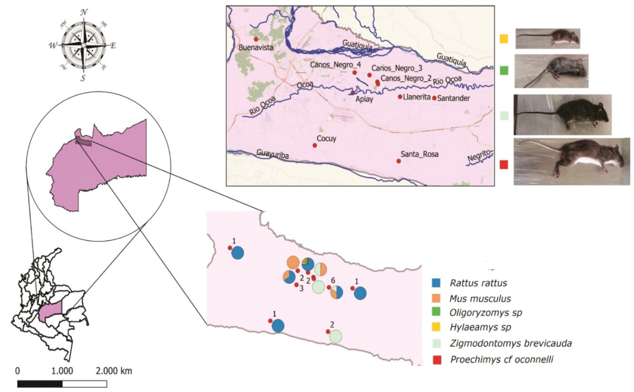

Figure 2. Distribution of small rodents in peri-urban and rural areas of the municipality of Villavicencio.

Tabla 3. Rodent species with morphometric data.

Family	Subfamily	Identified species	Frequency	Weight (gr) X-DE	Total length (mm) X-DE	Body (mm) X-DE	Tail (mm) X-DE	Ear (mm) X-DE	Leg (mm) X-DE
Muridae	*Murinae*	*Rattus rattus*	60% (30)	60.6 (38.4)	284.2 (64.1)	127.6 (28.3)	155.2 (37.6)	19.3 (2.8)	30.2 (5.2)
		Mus musculus	16% (8)	19.2 (8.1)	186.1 (44.9)	86.6 (15.4)	93.3 (19.6)	14.6 (3.0)	21.5 (6.4)
Cricetidae	*Sigmodontinae*	*Zygodontomys brevicauda*	16% (8)	64.4 (15.5)	217.3 (34.3)	120.3 (10.6)	99.5 (28.6)	16.4 (3.5)	23.4 (2.1)
		Oligoryzomys sp.	4% (2)	60 (0)	291 (4.2)	132.5 (3.5)	158.5 (0.7)	22 (1.4)	31 (1.4)
		Hylaeamys (antes Oryzomys)	2% (1)	15.0 (0)	168 (0)	80 (0)	88 (0)	12 (0)	20 (0)
Echimydae	*Eumysopinae*	*Proechimys cf. oconnelli*	2% (1)	160.0 (0)	289 (0)	180 (0)	109 (0)	23 (0)	42 (0)
Total			**100%**						

X: Mean. DE: Standard Deviation.

DISCUSSION

The present study allowed us to determine the frequency of rodent species in rural and peri-urban areas of the municipality of Villavicencio, Meta. However, no Hantavirus and Arenavirus species were detected in the collected specimens.

Anthropogenic influence on landscapes has increased rapidly in the last century with population growth. These changes have led to the disruption of biotic systems with subsequent direct and indirect impacts on human and wildlife animal populations(21).

Villavicencio is a municipality that has gone through significant changes in land use, which has led to an increase in the number of human settlements in the region, disturbing the ecology of wildlife animals and allowing the displacement and extension of others, such as rodents that have great adaptability (1,21). This study presents an initial effort to describe, visualize and map wild and synanthropic rodent species in peri-urban and rural areas of the municipality of Villavicencio.

The results obtained in this work regarding rodent species are the first to be reported in this municipality of the Colombian Orinoquia.

Rattus rattus and *Mus musculus* were previously reported as synanthropic rodents (7). However, it is essential to include species such as *Zygodontomys brevicauda*, *Hylaeamys* (formerly *Oryzomys*), *Proechimys oconnelli*, and *Oligoryzomys sp* in these areas of the municipality, documented in other regions of the country (2).

Olygorizomys sp (Pygmy Rice Rat) and *Hylaeamys sp* are distributed from northeastern Mexico to the extreme south of Chile and Argentina. In contrast, *Zygodontomys* (cane rat) from southeastern Costa Rica along Panama to Colombia, Venezuela, Guyana, and northern Brazil are mainly found in forests, mountains, grasslands, and wetlands (22).

Some researchers have also evidenced the interaction between wild and synanthropic rodents in their maintenance of enzootic cycles with other mammals before transmitting different etiological agents of importance in human health, such as *Leptospira sp, Mamarenavirus, Orthohantavirus, Yersinia pestis*, among others (15,23). Figure 2 shows the interaction between the synanthropic rodents *R. Rattus* and *M. musculus* with the wild ones captured in the field *Z. brevicauda*, *Oligoryzomys sp*, *Hylaeamys*, and *P. oconnelli*. The latter are primarily associated with diseases of public health, such as hemorrhagic fevers due to hantaviruses and Arenavirus (24,25,26).

The present study describes the spatial distribution of mammalian hosts, particularly small rodents, allowing us to show the richness, diversity, and population dynamics between rodent species in the different geographical areas of Villavicencio. These are necessary to determine the ecological role they play in the circulation of pathogens of public health importance.

The negative results found for Hantavirus and Arenavirus are encouraging in the captured populations of rodents from Villavicencio. However, it does not imply an absence of viral circulation because it is likely that the low number of specimens captured in the present study does not show the magnitude of the circulation of the analyzed microorganisms. Additionally, molecular analyses only allow us to infer that at the time of study of the specimens, no active infection of microorganisms was found.

In other regions of Colombia, studies have been carried out on rodents to determine species of Hantavirus and Arenavirus. Castelar et al. in 2017 found in urban synanthropic rodents a seroprevalence of 10% (8/80) against the lymphocytic choriomeningitis virus (LCMV) in the municipality of Sincelejo, Colombia. Of the 8 Seropositive rodents, only one could be identified by molecular markers in brain tissue (27). Montoya et al. in 2015 found molecular markers of Hantavirus in 7 lung tissue samples from rodents from Necoclí-Antioquia. However, the virus was not cultured from the samples (28). In the first seroprevalence studies in 2006 on Hantavirus and Arenavirus in Colombia, Alemán et al, found seroprevalences for Hantavirus antigens of 2.1% (7/336) in different municipalities of Córdoba. Mattar et al. 2011, reported a seroprevalence for Arenavirus of 1.1% (2/210) in rodents of the Sigmodontinae family (29). In 2016, Sánchez et al. diagnosed three cases of hantaviruses in patients with the undifferentiated febrile syndrome in the department of Meta, demonstrating the presence of the virus in the study region(30).

Although the presence of Hantavirus and Arenavirus in the lung could not be determined in the present study, these viruses could be found in other tissues (27), which could serve for new searches for these agents in different organs. In addition, it must be considered that the heavy annual rains in the municipality of Villavicencio during the trapping periods did not allow a more significant number of catches (9). This climatological variable could limit the detection of viruses. Therefore, the study's negative results do not rule out the presence of viral agents in the disturbed ecosystems of the municipality of Villavicencio and could contribute to the surveillance of hemorrhagic diseases transmitted by vectors that act as reservoirs.

Conflict of interest

The authors of this article declare that there is no conflict of interest.

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