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Clinical characteristics and use of antibiotics in a group of patients with snake bites in Colombia

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Abstract

Introduction: Millions of snake bites occur worldwide each year. Clinical practice guidelines generally do not recommend the use of prophylactic antibiotics.

Objective: To determine the sociodemographic, clinical, and pharmacological variables and the use of antibiotics in a group of patients with snake bites in Colombia.

Methods: A retrospective cross-sectional study was carried out. Patients affiliated with a Colombian health insurer who presented with snake bites between 2015 and 2022 were included. The cases were identified from the National Public Health Surveillance System. Sociodemographic, clinical and pharmacological variables were identified. Descriptive and bivariate analyses were performed.

Results: A total of 643 patients were analyzed, with a median age of 30.8 years, and 74.7% were men. The most frequently identified genus of snake was *Bothrops* (88.8%), and most incidents were classified as mild ophidian accidents (61.6%). A total of 59.7% of patients received snake antivenom. A total of 13.8% and 2.2% of the patients had cellulitis or abscesses, respectively. A total of 63.5% received antibiotics (50.6% for prophylaxis and 12.9% for treatment), especially cephalexin (25.9%), and most of the antibiotic management was considered inappropriate (91.7%).

Conclusion: Most patients with snake bites received antibiotics, especially for prophylactic purposes, a clinical behavior that goes against current evidence. The use of antibiotics with an unsuitable spectrum for the microorganisms that are usually found in the wounds of these patients is frequent. The development of local clinical practice guidelines is required to help reduce the overprescription of antibiotics, as the excessive use of antimicrobials is the main determinant of antimicrobial resistance.

Keywords: antibacterial agents, cephalexin, Colombia, inappropriate prescription, snake bites

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Introduction

An ophidian accident is an injury resulting from the bite of a snake.[1] Snakes may or may not be poisonous. Snakes that inoculate venom produce local or systemic alterations, a condition called ophidiotoxicosis.[1] Ophidiotoxicosis is a major public health problem in the developing world.[2] This is a major cause of morbidity and mortality, especially in the warmer areas of the tropics and subtropics, such as sub-Saharan Africa, South and Southeast Asia, and Latin America.[2] According to the World Health Organization (WHO), approximately 5.4 million snake bites are reported each year, 1.8–2.7 million cases are

classified as ophidiotoxicosis, and 80,000–140,000 deaths occur.[3] The incidence of ophidian accidents in Colombia is between 7.0 and 10.8 cases per 100,000 inhabitants, and the fatality rate is 0.6–1.0%.[4,5] The most medically important snake species in the country are grouped into the families *Viperidae* and *Elapidae*.[5] The family *Viperidae* is represented by the genera *Bothrops*, *Crotalus* and *Lachesis*.[5] The family *Elapidae* includes the genera *Micrurus* and *Pelamis*.[5] In Colombia, bothropic accidents represent 80–85% of all ophidian accidents caused by poisonous snakes.[1]

The initial management of patients who present with ophidian accidents consists of immobilization of the body, especially of the bitten limb, to reduce the spread of the venom; compresses are applied to the wound, the airway is monitored and protected, and frequently supplementary oxygen, IV fluids and pain relievers are administered.[2] Specific management is carried out through the administration of snake antivenom, which is the only effective means of neutralizing the systemic effects of snake bite poisoning.[2,6] In addition, treatment also involves the management of local and systemic complications.[6] Secondary infections caused by snake bites are frequent, for which antibiotics with coverage of gram-positive, gram-negative and anaerobic bacteria are indicated.[6] However, the use of prophylactic antimicrobials to prevent infections caused by snake bites is not widely recommended.[6–8]

The Colombian Health System offers universal coverage to the entire population through two affiliated regimes, the contributory regime that is paid by workers and employers and the subsidized regime that is responsible for the insurance of all people without the ability to pay and includes a benefit plan that covers snake antivenom, medications (e.g. antibiotics, analgesics, etc.) and a significant number of surgical procedures that patients with ophidian accidents may require. In the country of Colombia, there are some studies on the characterization of patients who have experienced snake bites[4,9] and reports from the National Institute of Health with general data regarding ophidian events and adherence to the clinical practice guide,[5] but the use of antibiotics in this group of patients has not been addressed.[4,5,9] Consequently, the present study was aimed to determine the sociodemographic, clinical, and pharmacological variables and the use of antibiotics in a group of patients with snake bites in Colombia.

Materials and methods

Study design and patients

A retrospective cross-sectional study was carried out on patients who presented with snake bites. The cases were identified from the notifications of snake bites made to the National Public Health Surveillance System. Patients affiliated with a health insurer in the country (Salud Total EPS, Bogotá, Colombia) were included. This insurer serves a population of over 3.8 million people distributed in most regions of Colombia and affiliated with both the contributory regime (85.0% of users) and subsidized regime (15.0%) of the Colombian Health System.

Patients of any age, sex, and city of origin who reported a snake bite between 1 January 2015 and 30 April 2022, were eligible. The consultation date was considered the index date for each patient, and the drugs, vaccines and supplies dispensed by the logistics operator (Audifarma SA, Pereira, Colombia) were identified.

Variables

Based on the information obtained from the notification and dispensing records, a database was designed that allowed the following groups of variables to be collected:

- Sociodemographic: sex, age, race, occupation, affiliation regime (contributory or subsidized) and place of origin, which was categorized according to the regions of Colombia, considering the classification of the National Administrative Department of Statistics (DANE) and the regions of Bogotá-Cundinamarca, Caribbean, Central, Eastern, Pacific and Amazon-Orinoquía.
- Clinics:
  - Characteristics of the snake: genus (*Bothrops*, *Crotalus*, or *Micrurus*, among others) and common name (mapaná, X, and padlock head, among others)
  - Location of the bite: head, extremities, fingers, thorax, abdomen, among others
  - Symptoms/signs: local (pain, edema, ecchymosis, erythema, blisters, bruises, and paresthesias, among others) and systemic (emesis, muscle weakness,

headache, vertigo, and bleeding, among others)
    - Complications: local (cellulitis, abscess, necrosis, and compartment syndrome, among others) and systemic (anemia, shock, ventilatory failure, and bleeding, among others)
    - Severity of the ophidian accident: no poisoning and mild, moderate or severe poisoning
    - Comorbidities: identified from the main and secondary diagnoses reported using the codes of the International Classification of Diseases, version 10.
- Nonpharmacological management:
    - Nonmedical practices: potions, prayers, herbal plasters, and mouth suction, among others
    - Type of initial care: tourniquet, immobilization, incision, and puncture, among others
- Pharmacological management:
    - Snake antivenom
    - Analgesics: acetaminophen, dipyrone, opioids (tramadol, codeine, others), nonsteroidal anti-inflammatory drugs-NSAIDs (ibuprofen, diclofenac, naproxen, others)
    - Antibiotics: Indication (treatment of bacterial superinfections at the time of care or for prophylaxis). Manipulation of the wound with nonsterile elements was considered an adequate indication for antibiotic prophylaxis.[6] The recommended antibiotics for treatment or prophylaxis were amoxicillin/clavulanic acid, ampicillin/sulbactam, cefotaxime, ceftazidime, piperacillin/tazobactam, gentamicin, amikacin and ciprofloxacin.[6] Their use in unapproved indications or when the prescription of antibiotics was different from those recommended was established as inappropriate use of antibiotics.[6]
    - Others: Systemic glucocorticoids (dexamethasone, prednisolone, and betamethasone, among others) and antihistamines (loratadine and hydroxyzine, among others)
    - Comedications: In the 90 days prior to the index date, such medications were grouped into the following categories: antidiabetics, antihypertensives and diuretics, lipid-lowering agents, antiulcer drugs, antidepressants and anxiolytics, and bronchodilators, among others.

Ethical statement

The protocol was endorsed by the Bioethics Committee of the Technological University of Pereira in the category of "research without risk" (approval code: 94-091221). The principles of confidentiality of information established by the Declaration of Helsinki were respected.

Data analysis

The data were analyzed with the statistical package Statistical Package for Social Sciences (SPSS) Statistics, version 26.0 for Windows (IBM, USA). Descriptive analysis was performed with frequencies and proportions for the qualitative variables and measures of central tendency and dispersion for the quantitative variables through medians and interquartile ranges. The comparison of quantitative variables was performed using the Mann–Whitney U test and X^2 or Fisher's exact test for categorical variables. The level of statistical significance was established at $p < 0.05$.

Results

A total of 643 patients distributed in 220 different cities were identified. A total of 74.7% were men, and the median age was 30.8 years (range: 0.0–91.0 years). A total of 20.5% ($n = 132$) were under 18 years old, 49.1% ($n = 316$) were between 18 and 39 years old, 25.5% ($n = 164$) were between 40 and 64 years old and 4.8% ($n = 31$) were 65 years old or older. Most of the patients were mestizo, affiliated with the contributory health system, lived in a municipal seat in the Caribbean region and were engaged in agricultural activities at the time of the ophidian accident (Table 1).

A total of 66.7% ($n = 429$) of the patients were able to identify the genus of the snake, which was most often *Bothrops* ($n = 381/429$; 88.8%), and the most recognized common name was "mapaná" ($n = 176$; 41.0%). The site of the bite was predominantly in the lower limbs, followed by the upper limbs. A total of 18.0% ($n = 116$) of patients performed nonmedical practices using herbal plasters

Table 1. Sociodemographic variables of 643 patients who presented with ophidian accidents in Colombia.

Variables	*n* = 643	%
Man	480	74.7
Age, median (IQR)	30.8 (21.1–43.3)	
Ethnicity	–	–
Mestizo	612	95.2
Black	24	3.7
Indigenous	5	0.8
Gypsy	2	0.3
Affiliation regime	–	–
Contributory	508	79.0
Subsidized	135	21.0
Geographic region	–	–
Caribbean	362	56.3
Eastern-Orinoquia-Amazon	134	20.8
Central	109	17.0
Bogota-Cundinamarca	22	3.4
Pacific	16	2.5
Area	–	–
Municipal head	299	46.5
Dispersed rural	226	35.1
Populated center	118	18.4
Activity	–	–
Agricultural activity	223	34.7
Domestic works	161	25.0
Walking on trails	122	19.0
Recreation	85	13.2
Aquatic activity	12	1.9

IQR, interquartile range.

(*n* = 38/116; 32.8%), potions (*n* = 29; 25.0%) or prayers (*n* = 22; 19.0%). In the initial care of the bite, the patients mainly used tourniquets (*n* = 165, 25.7%) and immobilized the limb (*n* = 84, 13.1%).

The most reported clinical manifestations were pain, edema, and erythema (Table 2). Infectious complications were the most frequent, including cellulitis (*n* = 89; 13.8%) and abscesses (*n* = 14; 2.2%). Most of the cases were classified as mild and moderate ophidian accidents (Table 2). A total of 59.7% (*n* = 384) received snake antivenom (mean: 3.9 ± 3.0 ampoules), 48.5% (*n* = 312) required hospitalization, and the fatality rate was 0.3% (*n* = 2).

Information on the dispensing of medications and the pathological antecedents of 170 patients was available. The main comorbidities identified were arterial hypertension (*n* = 38/170, 22.4%), diabetes mellitus (*n* = 11, 6.5%) and migraine (*n* = 10, 5.9%). A total of 73.5% (*n* = 125) had taken medications in the three months prior to the ophidian accident, mainly analgesics and anti-inflammatories (*n* = 92; 54.1%), antiulcer remedies (*n* = 27; 15.9%), and antihypertensives and diuretics (*n* = 25; 14.7%). In the care of the ophidian accident, 64.1% (*n* = 109) of the cases were managed with analgesics and 63.5% (*n* = 108) with antibiotics, mainly for prophylaxis (*n* = 86; 50.6%) and to a lesser extent for the treatment of concomitant infections (*n* = 22; 12.9%) (Table 3). Of the patients who were prescribed antibiotics, 91.7% (*n* = 99/108) of the treatments were considered inappropriate because they had no indication for prophylaxis or because the antibiotic scheme was not recommended in the clinical practice guidelines (Table 3).

Bivariate analysis

The group of patients who received antibiotic prophylaxis came in a greater proportion from the Caribbean region and had fewer comorbidities. In addition, these patients had their wounds washed less frequently but received more incisions and required more prescriptions of pain killers (Table 4).

Discussion

This study revealed that snake bites are caused primarily by the genus *Bothrops* and predominantly affect young adult males. Snake antivenom was used in more than half of the cases. The use of antibiotics was very frequent, and such drugs were used mainly for prophylaxis. Inappropriate use was found in more than 90% of the cases. Understanding

the use of antibiotics promotes their appropriate application and reduces their abuse or misuse.[10] The irrational use of medicines is a critical problem in different countries.[11] The WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately.[11]

The median age of the patients was similar to that found in Australia (33 years)[12] and another study from Colombia (31.7 years)[4] but lower than that reported in other countries (41.0–52.0 years),[13–16] with a predominance of men, as identified in the different studies (59.3–80.8%).[4,12–25] In this cohort of patients, the genus of the snake that was most identified was *Bothrops*, which is consistent with the epidemiological surveillance data of the country.[4,5] A third of all patients could not identify the genus of the snake, a difficulty that also occurs in other countries but in higher proportions (49.0–54.7%).[13,14,18] Its recognition is important since the microorganisms present in the oral cavity of snakes differ depending on the species,[26] and this may have therapeutic implications.[26] The wounds occurred mainly in the lower limbs, and the patients reported predominantly pain and edema in the bite area, which is consistent with what has been reported in the literature.[4,12–14,18,21,22,25,27]

The use of traditional practices and tourniquets were common behaviors in the out-of-hospital management of some patients, which is consistent with what has been described in other communities.[5,7,9,22,23,25] However, these approaches have not proven effective and can lead to complications.[2] The ophidian accident was classified in most cases in the mild or moderate category, which is in line with that reported in other international studies (73.6–97.2%)[7,13,14,19,20,22] and national studies (79.9–93.7%).[4,5,9] The proportion of patients classified as having severe ophidian accidents was low (2.6%), similar to that found in Panama and South Korea (0.8% and 2.8%, respectively),[18,19] but contrasts with other publications in which the prevalence was much higher (10.6–26.2%).[9,13,14,20,21] Snake antivenom was used in the majority of patients, which is consistent with national epidemiological surveillance reports[4,5] and international reports.[13,14,17,18,21,22,25] In pain management, the use of analgesics such as acetaminophen or opioids is recommended.[2] However, approximately one-third of patients received NSAIDs, which should be avoided because of the increased risk of bleeding.[2]

Table 2. Clinical variables of 643 patients who presented with ophidian accidents in Colombia.

Variables	*n* = 643	%
Wound location	–	–
Lower limbs	372	57.9
Upper members	171	26.6
Fingers	84	13.1
Others	16	2.4
Local manifestations	597	92.8
Pain	520	80.9
Edema	427	66.4
Erythema	245	38.1
Paresthesia	102	15.9
Ecchymosis	75	11.7
Systemic manifestations	200	31.1
Nausea	118	18.4
Emesis	49	7.6
Muscular weakness	40	6.2
Vertigo	39	6.1
Headache	21	3.3
Complications	–	–
Local	109	17.0
Systemic	9	1.4
Severity of the ophidian accident	–	–
No poisoning	66	10.3
Mild	396	61.6
Moderate	164	25.5
Severe	17	2.6

The proportion of patients with bacterial infections secondary to snake bites is heterogeneous.[4,12–18,20,21,24,27] In this cohort of patients, the rate of bacterial infections was similar to that found in Costa Rica (14.0%),[20] while the incidence was lower in countries such as Australia (1.0%),[12] Panama (6.1%),[18] Thailand (6.5%)[24] and India (6.7%)[27] and highest in another study in

Table 3. Pharmacological variables of 170 patients who presented with ophidian accidents in Colombia.

Variables	*n* = 170	%
Analgesics	109	64.1
Acetaminophen	60	35.3
Naproxen	36	21.2
Tramadol	29	17.1
Diclofenac	25	14.7
Dipyrone	6	3.5
Antibiotics	108	63.5
Cephalexin	44	25.9
Clindamycin	20	11.8
Ciprofloxacin	12	7.1
Ampicillin/sulbactam	10	5.9
Cephadrine	10	5.9
Cephalothin	10	5.9
Ceftriaxone	7	4.1
Dicloxacillin	7	4.1
Crystalline penicillin G	5	2.9
Trimethoprim/ sulfamethoxazole	4	2.4
Amikacin	3	1.8
Ampicillin	3	1.8
Cefazolin	2	1.2
Gentamicin	2	1.2
Oxacillin	2	1.2
Sultamycin	2	1.2
Amoxicillin/clavulanate	1	0.6
Azithromycin	1	0.6
Doxycycline	1	0.6
Benzathine penicillin G	1	0.6
Systemic glucocorticoids	23	13.5
Systemic antihistamines	15	8.8
Indication of the antibiotic	-	-
Prophylaxis	86	50.6
Treatment	22	12.9
Inadequate prescription of antibiotics (*n* = 108)	99	91.7
Inadequate indication of the antibiotic	84	77.8
Inadequate selection of the antibiotic scheme	77	71.3

Colombia (22.4%),[4] Taiwan (22.5–28.0%),[15–17] Brazil (23.3%),[21] and French Guiana (32.0–32.3%).[13,14] However, in this report and in other studies, the use of antibiotics predominated widely (63.5% *versus* 80.2–94.6%).[18,20,22,25,27] Therefore, the prescription of antimicrobials was not only for the treatment of secondary infections but also for preventive management (prophylaxis). With this indication, antibiotics were used to treat half of the patients, consistent with other reports (44.2–75.0%).[15,17] Evidence does not support the use of empirical antibiotics to prevent a secondary infection after a snake bite.[7,8] Therefore, clinical practice guidelines do not recommend this medical practice.[1,6]

In patients with cellulitis or abscesses after a snake bite, antibiotic therapy should be guided by a culture of the wound's discharge and sensitivity testing whenever possible.[28] Empirical treatment should cover gram-positive aerobic bacteria (e.g. *Staphylococcus aureus* and *Enterococci* spp), gram-negative aerobic bacteria (e.g. *Morganella morganii*, *Escherichia coli*, *Klebsiella* spp, *Salmonella* spp and *Enterobacter* spp), and anaerobic bacteria (e.g. *Peptostreptococcus* spp and *Bacteroides fragilis*) while awaiting culture results.[6,28] The antibiotic prescription patterns found in the different studies are variable.[14,15,18,20,21,27] Thus, penicillin G predominated in Panama and Costa Rica,[18,20] amoxicillin/clavulanic acid in French Guiana,[14] ampicillin in India,[27] cefadroxil in Taiwan[15] and clindamycin in Brazil,[21] while in this report, first-generation cephalosporins were mainly used, especially cephalexin. Many of these antibiotics do not adequately cover the microorganisms present in the oral cavity of snakes.[6] There are no studies in Colombia regarding the resistance and

Table 4. Comparison of sociodemographic, clinical, and treatment variables among patients with snake bite who did or did not receive antibiotic prophylaxis in Colombia.

Variables	With prophylaxis		Without prophylaxis		*p*
	n = 86	%	*n* = 62	%	
Sociodemographic	–	–	–	–	–
Man	56	65.1	38	61.3	0.633
Age, median (IQR)	30.4 (17.1–48.8)		29.0 (18.9–52.2)		0.725[a]
Origin Region Caribbean	63	73.3	30	48.4	0.002
Contributory regime	70	81.4	53	85.5	0.512
Clinics	–	–	–	–	–
Comorbidities	24	27.9	35	55.5	<0.001
Arterial hypertension	11	12.8	25	40.3	<0.001
Diabetes mellitus	1	1.2	10	16.1	0.001[b]
Bite on lower limbs	55	64.0	33	53.2	0.190
Local manifestations	82	95.3	54	87.1	0.070
Pain	76	88.4	49	79.0	0.122
Edema	58	67.4	35	56.5	0.172
Erythema	36	41.9	24	38.7	0.700
Systemic manifestations	22	25.6	19	30.6	0.497
Nausea	14	16.3	9	14.5	0.770
Emesis	8	9.3	6	9.7	0.939
Muscular weakness	4	4.7	5	8.1	0.492[b]
Severity of the Ophidian Accident	–	–	–	–	–
No poisoning	7	8.1	6	9.7	0.744
Mild	54	62.8	40	64.5	0.830
Moderate	20	23.3	16	25.8	0.721
Severe	5	5.8	0	0.0	0.075[b]
Out-of-hospital management	–	–	–	–	–
Tourniquet	19	22.1	10	16.1	0.367
Limb immobilization	12	14.0	10	16.1	0.714
Washed	3	3.5	9	14.5	0.029[b]
Incision	11	12.8	1	1.6	0.014[b]
Inpatient management	–	–	–	–	–
Analgesics	64	74.4	29	46.8	0.001

(Continued)

Table 4. (Continued)

Variables	With prophylaxis		Without prophylaxis		*p*
	n = 86	%	*n* = 62	%	
Snake antivenom	50	58.1	28	45.2	0.119
Systemic glucocorticoids	12	14.0	6	9.7	0.432
Systemic antihistamines	8	9.3	6	9.7	0.939

[a]Mann–Whitney *U* test.
[b]Fisher's exact test.
IQR, interquartile range.

sensitivity patterns of the microorganisms involved in infections caused by snake bites. This makes it difficult to establish suitable recommendations for the empiric prescription of antibiotics. However, it is common in the literature to find resistance to first- and second-generation cephalosporins, aminopenicillins with beta-lactamase inhibitors, and oxacillin, among others.[14–16]

In Colombia, the use of antibiotics for unapproved indications is common,[29–31] a condition that leads to adverse clinical (increased length of hospital stay, morbidity, mortality, and antimicrobial resistance) and economic (increased costs of care) effects.[32] Thus, it is important to highlight that, in this study, the inappropriate use of antibiotics prevailed in most patients. These findings are consistent with a Colombian study on the use of antibiotics in patients with dog or cat bites, in which it was found that inappropriate use occurred in 72.0% of cases, and 49.2% had no indication for antibiotic prophylaxis.[29] Additionally, it has been established that the inappropriate use of antibiotics is common, both in the outpatient setting (8.0–100%)[33] and in hospitals (14.1–78.9%).[34] The great importance of the above finding is that the improper and excessive use of antimicrobials is the main factor that determines the appearance of drug-resistant pathogens.[35]

Some limitations should be considered when interpreting these results. The data were obtained from an insurer of individuals participating mainly in the contributory regime of the Colombian health system; consequently, these findings may not be extrapolated to people without the same affiliation or the dependents of other insurers. In addition, for some variables, information on the total number of patients was not available, especially in relation to the dispensing of medicines, because in the dispersed areas of the country, other logistical operators are responsible for their delivery. There was no access to data from paraclinical studies. Moreover, patient follow-up could not be carried out due to lack of this information; thus, the effectiveness of antibiotic prophylaxis could not be evaluated. However, this analysis, as a starting point, shows the excessive use of antibiotics in patients who have experienced an ophidian accident, and the medical community should be alerted to this finding.

Conclusion

With these results, we can conclude that the most commonly received antibiotics, especially when applied for prophylactic purposes, are a clinical approach that goes against current evidence. In addition, the use of antibiotics with an unsuitable spectrum for the microorganisms that are usually found in the wounds of these patients is frequent. Studies are necessary to characterize the microorganisms present in the wounds caused by snake bites, as well as the pattern of sensitivity and resistance, to thereby establish national recommendations on the appropriate use of antibiotics. Moreover, the development of local clinical practice guidelines is required to help reduce the overprescription of antibiotics. The excessive use of antimicrobials is the main determinant of antimicrobial resistance. These findings can be useful for health care, academic and scientific personnel in making decisions regarding the risks their patients face and can help strengthen the appropriate use of antibiotics as a means of reducing resistance to these antibiotics.

Declarations

Ethics approval and consent to participate

The protocol was approved by the Bioethics Committee of the Universidad Tecnológica de Pereira (Technological University of Pereira) in the category of risk-free research (Code: 02-070620). The ethical principles established by the Declaration of Helsinki were respected. According to the regulations of Colombia (Resolution 8430 of the Ministry of Health of 1993), observational studies that are without risk and involve information obtained only from databases do not require informed consent and must respect the principles of confidentiality of the information.

Consent for publication

Not applicable.

Author contributions

Luis Fernando Valladales-Restrepo: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Writing – original draft.

Ana Sofia Rojas-Ramirez: Data curation, Formal analysis, Writing – original draft.

Melba Jasbleidy Santander-Pai: Data curation, Formal analysis, Investigation.

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Jorge Enrique Machado-Alba: Conceptualization, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

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