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Distribution of prevalence of *Strongyloides stercoralis* in Peru (1981-2010): an exploratory study

Distribución de la prevalencia de *Strongyloides stercoralis* en el Perú (1981-2010): un estudio exploratorio

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Resumen

La estrongiloidosis es endémico en regiones tropicales y subtropicales de Latinoamérica. En Perú, el impacto de *Strongyloides stercoralis* en salud pública es desconocido. El objetivo del presente estudio es describir la distribución espacial y temporal de la prevalencia de *S. stercoralis* en Perú entre 1981 y 2010; y las poblaciones más afectadas. Se realizó una búsqueda de los estudios epidemiológicos en las base de datos de LIPECS, LILACs, Scielo Peru, MEDLINE y Google Scholar. Los estudios incluidos en el estudio fueron aquellos que reportaban prevalencia de *S. stercoralis* usando cualquier técnica parasitológica. Entre 1981 y 2010, la tasa de prevalencia global fue 6,3 %. Un total de 3 695 personas fueron reportadas con *S. stercoralis* en durante los 30 años. De 1981 a 2001, un total de 3 013 sujetos tuvieron S. stercoralis en heces que representa una prevalencia global de 6,6 %. De 2002 a 2010, un total de 676 sujetos tuvieron *S. stercoralis* en heces, representando una tasa de prevalencia global de 5,1 %. Se notó una reducción en la prevalencia global durante los 30 años excepto en la región de la costa, hallazgo que merece mayor investigación. En conclusión, *S. stercoralis* es hiperendémico en varias zonas de la selva del Perú con menor grado en la costa y sierra. Futuros estudios epidemiológicos deben usar técnicas diagnosticas altamente sensibles para la detección de larvas de *S. stercoralis* tales como la técnica de Baermann modificada en copa o el cultivo de agar en placa para evitar la subestimación de esta parasitosis.

Palabras clave: Estrongiloidiasis | Estrongiloidiasis/epidemiología | Strongyloidiasis/ prevención & control | Strongyloides stercoralis | Perú.

Abstract

Strongyloidiasis is endemic in tropical and subtropical regions of Latin America. In Peru, the impact of *Strongyloides stercoralis* in public health is unknown. The objective of the present study is to describe the spatial and temporal distribution of the prevalence of *S. stercoralis* in Peru between 1981 and 2010, and the most affected populations. A search for epidemiological studies was performed in the database of LIPECS, LILACs, Scielo Peru, MEDLINE and Google Scholar. The studies that reported prevalence of *S. stercoralis* by using any parasitological technique were included. Between 1981 and 2010, the global prevalence rate was 6.3 %. A total of 3,695 people were reported with *S. stercoralis* in stools during the last 30 years. From 1981 to 2001, a total of 3,013 subjects had *S. stercoralis* in stools that represents a global prevalence rate of 6.6 %. From 2002 to 2010, a total of 676 subjects had *S. stercoralis* in stools that represents a global prevalence rate of 5.1 %. A global reduction of prevalence was noted during the last 30 years except in the Coastal region, which deserves further research. In conclusion, *S. stercoralis* is hyperendemic in many areas of the rainforest of Peru into a lesser extent in the coast and Andean region. Future epidemiological studies should use highly sensitive diagnostic techniques for *S. stercoralis* larvae detection such as Modified Baermann's Technique or Agar-plate Culture to avoid underestimating this parasitosis.

Key words: Strongyloidiasis | Strongyloidiasis/epidemiology | Strongyloidiasis/ prevention & control | Strongyloides stercoralis | Peru.

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Introduction

Strongyloides stercoralis is a nematode that can infect humans by causing the disease strongyloidiasis.[1] An estimate of 30-100 million people are infected in tropical and subtropical regions worldwide.[2] *S. stercoralis* has unique features in both pathogenesis and life cycle. It can survive in humans for years under a singular mechanism called autoinfection, replication of the adult form into the intestines allowing perpetual infection. The filariform larvae can migrate from the intestine throughout multiple organs causing the hyperinfection syndrome and dissemination and it can cause high morbidity and mortality (~69 %) especially in the immunocompromised host.[3]

In endemic areas, risk factors for acquiring the infection are frequent bathing in rivers and walking barefoot mainly.[4] Several methods have been described for detection of *S. stercoralis*, but its diagnosis still remains a challenge.[3] Serological tests by antibody detection may indicate an old or past infection, but an unequivocal diagnosis of *S. stercoralis* is made when larvae are found in fresh stools. [1,3] The most sensitive parasitological techniques are the agar plate culture and modified Baermann's technique (MBT).[5,6] Preserved stool samples may decrease sensitivity because alive larvae are required to migrate in water or agar culture.[7] The drug of choice for strongyloidiasis is ivermectin;[8,9] or thiabendazole, as an alternative.[10]

Disclosing endemic areas and the most susceptible populations affected by *S. stercoralis*, will undoubtedly contribute in the development of prevention and control measures. It is well known the association between severe strongyloidiasis and those coinfected with the human T-cell-lymphotropic virus 1 (HTLV-1), endemic in Peru.[11] Moreover, HTLV-1 is highly frequent in patients who develop *S. stercoralis* hyperinfection in Peru.[12] This syndrome can also be caused by *S. fuelleborni*,[13] first reported in Peru in 2000.[14] Important advancements in diagnosis and immunology of *S. stercoralis* have evolved in the last years in Peru.[15] Endemic areas are present in developing countries, but cases have also been reported in industrialized countries due to immigrations.[3,16] After finding 6 % of 83 Latin-American patients before organ transplantation with positive serology for *S. stercoralis* in the United States, pre-screening of people from Latin America for strongyloidiasis was suggested because profound immunosuppression is required after transplantation.[17]

To the best of our knowledge, little evidence is available about *S. stercoralis* and its public health impact in Peru. The objective of the present study is to report the spatial and temporal distribution of prevalence along with the most affected populations by *S. stercoralis* in Peru.

Material and methods

Search strategy. A search for epidemiological studies was performed in the following databases:

LIPECS
http://www.upch.edu.pe/vrinve/dugic/

LILACs
http://lilacs.bvsalud.org/

Scielo Peru
http://www.scielo.org.pe
http://www.upch.edu.pe/vrinve/dugic/

MEDLINE
http://www.pubmed.com

Google scholar
http://scholar.google.com/

The combined terms used in Spanish or English for the searching were "*S. stercoralis*", "Peru", "*stercoralis*", "Prevalencia/Prevalence", "Strongyloidosis/Strongyloidiasis". A manual search was carried out for the non-electronic publications, thesis, and book abstracts from local meetings. The studies from 1981 to 2001 were included from a previous publication[18], with some additional references.[19-21]

Furthermore, direct communication to authors was performed when needed.

Inclusion Criteria. Epidemiological studies published from 1981-2010 that had prevalence data of *S. stercoralis* in humans using any parasitological technique. We only included original studies performed in the general population independently of age, and carried out in a specific geographic location.

Statistical analysis. In order to minimize potential misclassification bias of endemic areas into low or high endemic regions, and given the variability in the detection rate of diagnostic tools as well as number of stool samples that could potentially affect prevalence rates, we arbitrarily nominated the endemic areas (provinces) in three groups separated by a large range of percentages: i) hyperendemic ≥ 10 %; ii) mesoendemic between 1 to 10 %; and, iii) hypoendemic < 1 %. This stratification according to the prevalence rates was performed with at least one study in children or adults or both. The results of one study with one or more communities were assumed to represent to the rest of the districts in a province, under the hypothesis that the prevalence was similar in the rest of the province. When more than one study within a province or between neighbor provinces independently of the year were present, the study with the highest prevalence rate was considered for the final stratification analysis. A sub analysis was carried out to compare prevalence rates per region according to the diagnostic technique used. Comparison of proportions was performed using Chi-square. A *p*-value < 0.05 was considered level of significance. In addition, given the variability of diagnostic techniques used among studies per region and the need to reduce selection and misclassification bias, a comparison of the global prevalence per region and by diagnostic techniques was performed.

Results

Prevalence between 1981 and 2010. The global prevalence of *S. stercoralis* in all regions was 6,25 % (n total = 59 268; 95 % Confidence Interval (CI) =6,1 - 6,45). Overall, the prevalence rate in the coast was 4,2 % (n=26 173; 95 % CI =3,9 - 4,5), in the Andean region was 1,3 % (n=15 332; 95 % CI =1,1 - 1,4) and in the rainforest; 13,6 % (n= 17 763; 95 % CI =13,1 - 14,1). Results of prevalence rates per region between periods of 1981-2001 and 2002-2010 are showed in Table 1.

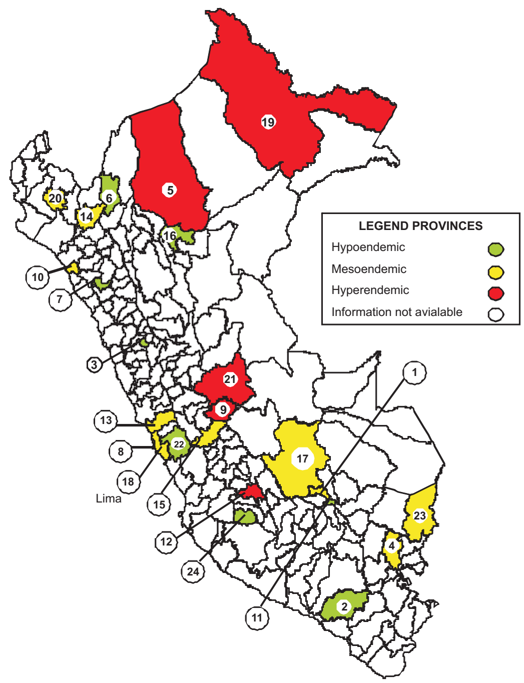
Prevalence from 1981 to 2001. Data from this period was analyzed from a report performed by the Ministry of Health in Peru in 2003,[18] and other studies included in this period were added.[19-21] A total of 45 653 subjects in 93 studies from 20 departments were included. The global prevalence rate was 6,6 %, ranging from 0,1 % to 61,7 %. A total of 3 013 subjects had larvae of *S. stercoralis* in the stools.

Prevalence from 2002 to 2010. In this period, a total of 12,999 subjects in 35 studies from 14 departments were included in the present study (Table 1; Figure 1).[22–51] A total of 683 cases had

Table 1. Global prevalence rates of *S. stercoralis* in Peru by cross-sectional studies published between 1981 and 2010.

Geographic region	1981-2010	1981-2001‡		2002-2010		p-value
	Global prevalence (%)	Sample (n)	Global prevalence (%)	Sample (n)	Global prevalence	
Coast	4.2	23,047	4.1	2,923	5.01	0.02
Andean	1.3	10,685	1.18	4,234	1.48	0.27
Rainforest	13.6	11,921	16.3	5,842	8.1	0.0001
Total	6.3	45,653	6.6	12,999	5.2	0.0001

‡ = Dates from References 18-21



Code	Province
1	Anta
2	Arequipa
3	Asunción
4	Azángaro
5	Alto Amazonas
6	Bagua
7	Cajabamba
8	Callao
9	Chanchamayo
10	Chiclayo
11	Cusco
12	Huamanga
13	Huaral
14	Jaén
15	Jauja
16	Lamas
17	La Convención
18	Lima
19	Maynas
20	Morropón
21	Oxapampa
22	Oyón
23	Sandia
24	Víctor Fajardo

Figure 1. Stratification of endemic areas of *S. stercoralis* in Peru (2002-2010).

S. stercoralis larvae in stools with prevalence rates ranging from 0,3 % to 39 % in Peru. Global prevalence for this period was 5,1 %. The population described in these studies was as follows: children, adults or general population. Overall prevalence rate in children was 1,96 % (n=3 054); in adults; 6,4 % (n=3 434); and in the general population; 6,2 % (n=6 511). In the studies that described the general population both children and adults together, it was not possible to analyze the data stratified by age. A summary of the studies from 2002 to 2010 is presented in Table 2.

Additional information. From a reference of the period 1981-2001,[(21)] additional information was included as supplemental data containing 13 studies during the period 1962-1975 (Table 3).[(21,52)] Out of 4 124 people included in these studies; 39,4 % had *S. stercoralis* larvae in stools by MBT, prevalences ranged from 0,6 % to 96,5 %. Most of these studies were applied in the rainforest.

Mapping *S. stercoralis* in Peru. The geographic distribution of *S. stercoralis* in Peru for the period 2002-2010 by endemicity per region was: in the coast, 5,0 % (n=2 923); Andean region, 1,5 % (n=4 234), and in the rainforest, 8,1 % (n=5 842) (p<0.001). Stratification of endemic areas of *Strongyloides* in this period is presented in Figure 1.

Prevalence by diagnostic techniques. Out of the studies collected from the period 2002-2010, a sub analysis of the prevalence rates stratified by diagnostic technique in each region was performed. By assuming each region has similar risk for transmission, this subanalysis could be the best approach to reality given the limitations in each study and heterogeneity among them. In the coast, the prevalence rates by direct smear test was 2,2 %, and by MBT was 5,2 % (p>0,05). In the Andean region, the prevalence rates by direct smear test was 4.9 %; by other techniques, including spontaneous sedimentation technique in tube (SSTT),

Table 2. Prevalence of *S. stercoralis* in Peru by cross-sectional studies published from 2002 to 2010.

Department	Province	Diagnostic test	Sample (n)	Prevalence (%)	Nº persons infected	Population	Year	Reference
Coast								
Callao	Callao	Direct smear/RST	89	2.2	2	General population	2002	22
Lambayeque	Chiclayo	MBT	388	1.5	6	Children	2002	23
Lima	Lima	MBT	217	6.9	15	Adults	2006	24
	Lima	MBT	2056	6.0	123	Adults	2009	25
	Huaral	MBT	173	1.1	2	Children	2007	26
Andean								
Ancash	Asunción	Direct smear test	706	0.3	2	General population	2007	27
Arequipa	Arequipa	RST	175	0.6	1	General population	2002	28
Ayacucho	Huamanga	SSTT	67	14	9	Children	2002	29
	Víctor Fajardo	Ritchie	312	0.32	1	General population	2005	30
Cajamarca	Jaén	Direct smear test	2000	7.3	146	General population	2003	31
	Cajabamba	Direct smear test	256	0.8	2	Adults	2009	32
Cusco	Cusco	Teleman	631	0.32	2	Children	2007	33
	Anta	Teleman/RST	143	1.2	2	General population	2002	34
Junín	Jauja	SSTT	96	1.1	1	Children	2002	35
	Jauja	SSTT	92	2.2	2	Children	2002	35
Lima	Oyon	Direct smear test	132	0.8	1	General population	2008	36
Piura	Morropon	Direct smear test	63	4.8	3	Children	2005	37
Puno	Azángaro	MBT	236	2.1	5	Children	2007	38
Rainforest								
Amazonas	Bagua	Teleman	1049	0.8	13	Children	2005	39
Cusco	La Convención	Direct smear test	1120	1.3	15	General population	2002	40
	La Convención	SSTT	142	7.0	10	Children	2006	41
Junín	Chanchamayo	MBT/Agar plate	113	21.6	24	General population	2003	42
	Chanchamayo	MBT	54	3.7	2	Children	2004	43
	Chanchamayo	MBT	400	14.8	59	General population	2009	44
	Chanchamayo	MBT	647	10.9	71	General population	2009	44
Loreto	Maynas	MBT	41	24.9	10	Adults	2002	45
	Maynas	MBT	792	8.7	69	Adults	2006	46
	Alto Amazonas	MBT/Culture	203	17.2	35	General population	2007	47
Pasco	Oxapampa	Harada-Mori	98	1.02	1	General population	2004	48
	Oxapampa	Culture	109	38.5	42	General population	2005	49
Puno	Sandia	MBT	72	1.4	1	Adults	2009	50
San Martín	Lamas	RST	264	0.5	1	General population	2002	51
Total			13 526		692			

SSTT: spontaneous sedimentation technique in tube; MBT: modified Baermann's technique; RST: rapid sedimentation technique.
For additional geographic information of studies between 1981 and 2001, see reference 15-20.

Table 3. Prevalence of *S. stercoralis* in Peru by cross-sectional studies published from 1962 to 1975 (Supplemental data)

Department	Province	Diagnostic test	Sample (n)	Prevalence (%)	Nº persons infected	Population	Year
Ancash	Pallasca	MBT	150	0.66	1	General population	1965
Cuzco	La Convención	MBT	240	49	118	General population	1964
Huánuco	Leoncio Prado	MBT	39	17.9	7	General population	1970
Junín	Chanchamayo	MBT	498	41.16	205	General population	1964
	Chanchamayo	MBT	89	32.5	29	General population	1970
Lima	Lima	MBT	188	5.8	11	Children	1964
Loreto	Maynas	MBT	254	48.03	122	General population	1975
Madre de Dios	Tambopata	MBT	198	96.5	191	General population	1964
Moquegua	Mariscal Nieto	MBT	483	0.2	1	General population	1964
Pasco	Oxapampa	MBT	263	43.73	115	General population	1963
Ucayali	Cnel. Portillo	MBT	226	36.72	83	General population	1962
Puno	Azángaro	MBT	281	1	3	General population	1964
San Martin	Rioja	MBT	1215	60	729	General population	1964
Total			4 124	39.4	1 615		

Data was obtained from references 21 and 51.

Ritchie's method and RST was 1,2 %; and by MBT was 2,1 % (p>0,05). In the rainforest, the prevalence rates by direct smear test was 1,3 %, by other techniques (including SSTT and RST) was 1,6 % and by MBT was 11,8 % (p<0,001) (Figure 2).

Discussion

We have found a global prevalence rate of *S. stercoralis* of 6,3 % throughout Peru during the period 1981-2010; which is higher than other similar studies performed in other countries in Latin America. In Brazil, after analyzing studies from 1990 to 2009 a global prevalence rate of 5,5 % was reported.[53] In Peru, six provinces were classified as hyperendemic areas and were located in the rainforest except one in the Andean region.

The global prevalence of *S. stercoralis* in the rainforest is statistically lower in the period 2002-2010 (8,1 %) than 1981-2001 (16,3 %). Perhaps, improvements in sanitary, hygienic and socioeconomic conditions may explain the lower rates. In another study, a decreased trend in the prevalence of *S. stercoralis* was also found from 11,7 % during 1970-1985; to 6 % during

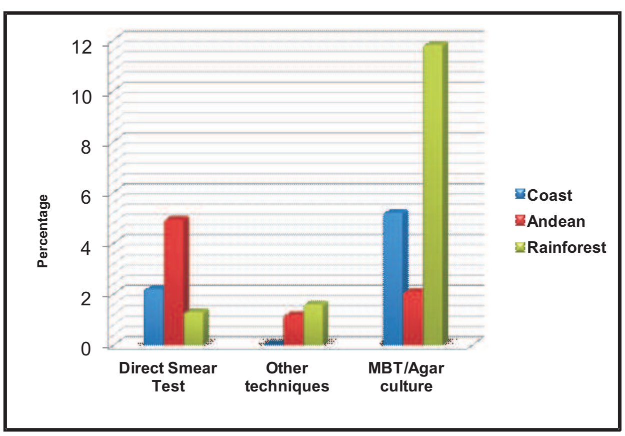


Figure 2. Impact of diagnostic technique on distribution of *S. stercoralis* according to the prevalence studies from 2002-2010 .

1990-1997. [54] In our study, supplemental data (period 1962-1975) showed a global prevalence of *S. stercoralis* about 39,4 % in the rainforest, ranging from 17,9 % to 96,5 %. These findings confirm the results from other studies which also showed that *S. stercoralis* is widely hyper-endemic in the rainforest.[18,55] In another multicentric study from the rainforest, *S. stercoralis* prevalence was higher even in villages (Puerto Maldonado, Sepahua y Nauta) from the Amazonic basin than those located at a higher altitude (700 meters above sea level) (Satipo and Rioja), closer to the Andean region.[56] Nonetheless, its prevalence can reach up to 70 % even in these low-level altitude rainforest areas.[57]

Among the number of diverse climate and microclimates present in Peru, the rainforest seems to have an optimal environment for the development of *S. stercoralis* life cycle; because it is humid, hot and rainy. In contrast, the Andean region may not have an optimal climate for the development of larval stages; because it is cold, dry and less rainy. As expected, lower prevalence rates were found in the Andean region (1,3 %) in this study when compared to the coast (4,2 %) and rainforest (13,6 %). Also, those prevalence rates between 1981-2001 and 2002-2010 periods in the Andean region did not change significantly (from 1,18 % to 1,48 %). Hypoendemic areas are widely distributed throughout the Andean region, in particular those located closer to the Pacific coast. If unexpected climatological events cause high rainy seasons such as ENSO (El Niño Phenomenon), without improving sanitary conditions or changing human behavior, the rate of endemicity can be invariably modified in proportion to the burden of larvae into the environment. Another factor in the dissemination of infectious diseases is mobilization of population between regions. Immigration from Andean to rainforest region is usually between rainy season (January-March) associated to agricultural activities,[58] which may be a risk factor for acquiring *S. stercoralis* while working in the rainforest and then returning to the place of origin after agriculture season is finished.

Conversely, the prevalence of *S. stercoralis* in the coast was significantly higher in recent than remote years (from 4 % to 5 %). Climatological conditions in the coast are more environmentally optimal for *S. stercoralis* development than those in the Andean region. A mesoendemic area for *S. stercoralis* was found in the coast in this study. Poor hygienic conditions may enable establishing a favorable microenvironment for larval stage development where parasite may become in closer proximity to humans and so keeping it infectious.[18] In fact, a study found *Strongyloides spp*. larvae in about 63 % of lettuce in large markets in Lima city [59], and in 20,2 % of vegetables (celery, spinach, leeks, among others) designated to Lima city[60].

Variability of prevalence rates may be explained by differences in sensitivity among the parasitological techniques applied in each study. In fact, in a subanalysis we found that prevalence rates varied significantly in the rainforest when different techniques were applied ($p < 0,05$), but this is not a breakthrough finding.[7] Factors including number of stools and sample preservation or transportation may be entertained as confounders. MBT showed higher statistically significant prevalence rates than other techniques in the rainforest or hyperendemic areas; but this difference was not significant in low-prevalent regions such as the coast and highlands. Interestingly, in the period of 1962-1975, MBT was used in all the 14 studies and the overall prevalence rate was 39,4 %; and up to 96,5 %; highest ever reported. Small modifications to the Baermann's Technique can increase the sensitivity to detect *S. stercoralis* larvae.[61] Last, *Rhabditis (Rhadbitiella) axei* is very similar to *S. Strongyloides* larvae and careful attention should be paid to avoid misinterpretation.[61]

Several limitations are present in this study. One of the most important is the heterogeneity of the studies regarding the diagnostic parasitological technique. Unfortunately, direct smear underestimates the prevalence rates.[7] Other limitations are small sample size, lack of randomization methods, population heterogeneity and disproportional number of studies per region. One could argue that the use of different parasitological techniques could be a limitation to compare studies or regions. The reason behind to include all studies, independently of the stool-based technique applied, was to analyze in detail the differences in prevalence rates by region (Figure 2) and to estimate the expected proportion of underestimation for *S. stercoralis*. In fact, we found that the use of direct smear as screening test for *S. stercoralis* when compared to the MBT or agar plate at a population-based level reduces the prevalence rates in about 58 %-88 %. Nevertheless, the objective of this study was to try developing a mapping for assessment of *S. stercoralis* endemic areas as an exploratory study for future projects. In addition, future studies might be needed to verify our results which remains informative. Ideally, a trend of the prevalence rates along the years should be performed in the same population in each village, using the same diagnostic parasitological technique in stools and stratified by age groups. A systematic review of prevalence studies about *S. stercoralis* in Peru may be considered to address this question.

In conclusion, *S. stercoralis* is endemic in all regions of Peru, hyperendemic in the rainforest, and less endemic in the Andean and coastal regions. The prevalence of *S. stercoralis* in the rainforest from 2002-2010 period was significantly lower than previous years. The use of the direct smear test underestimates the prevalence rates of *S. stercoralis* throughout Peru, and therefore the routine use of highly sensitive techniques are recommended when possible. A significant increase in prevalence rates was observed in the coast, which deserves further investigation. Finally, the occurrence of *S. stercoralis* throughout Peru and the potential adaptability of the parasite to other non-tropical regions, along with its unique characteristics of perpetual infection, invasion to multiple organs into the host and challenging diagnostic approaches; place *S. stercoralis* into a new dimension among the neglected tropical diseases of the world but in particular within Peru.

Conflict of interest:

None declared

Author's Contributions

Designed the study: LM, RC.
Data collection: LM, RC, JM, MC, AT.
Analyzed the data: LM, RC.
Interpreted the data: LM, RC, AT.
Drafted the manuscript: LM.
Critically revised the manuscript for intellectual content: LM, RC, JM, MC, AT.

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