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The effects of natural disasters on leishmaniases frequency: A global systematic review and meta-analysis

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ABSTRACT

Objectives: Natural disasters (NDs) may increase the outbreaks and transmissions of vector-borne diseases such as cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL). However, the relationship between leishmaniases and NDs has not yet been clearly established. Here, we systematically reviewed all reported articles in this field to answer whether NDs increase the frequency of leishmaniases.

Methods: All the related articles published during January 2000 till January 2020 were reviewed. Moreover, all NDs and the associated leishmaniases frequencies reports in 17 leishmaniases endemic countries were searched to find any ND-leishmaniases relationship.

Results: After the initial screening, 39 articles on ND-leishmaniases were selected and systematically reviewed. These articles showed different frequencies of CL in the endemic areas before and after NDs in some regions of Pakistan and Iran and in case of VL in Brazil, Ethiopia, and Sudan. After thorough deliberation, four studies for CL-ND and five studies for VL-ND relationships were selected for meta-analysis. The results showed increases in the leishmaniases incidences after NDs, although not robustly.

Conclusion: The lack of a strong leishmaniases-ND relationship could be attributed to the local compilations of such data in scattered regions of the endemic countries. Therefore, currently a substantial knowledge gap on leishmaniases-ND relationship is apparent.

1. Introduction

Natural disasters (NDs) often have a devastating impact on the public health of the stricken regions, especially in the developing countries. NDs often cause the destruction of the ecosystems, habitats and infrastructures, leading to displacements of large numbers of people to temporary safe shelters such as tents which are usually overcrowded and lack adequate standards of hygiene. Furthermore, NDs are followed by contamination of water supplies and hence increases in outbreaks of vector-borne and zoonotic diseases (Parekh et al., 2020). Leishmaniases are a collection of vector-borne diseases caused by *Leishmania* parasites and can be divided into several clinical forms. Two of the most prevalent and widespread clinical forms of leishmaniases are cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL) (Burza et al., 2018). According to the World Health Organization (WHO) reports, leishmaniases are localized in low and middle income countries (LMIC) of South-East Asia, Middle-East, North and Sub-Saharan Africa, and South America. The countries with the most CL cases are Afghanistan, Algeria, Brazil, Colombia, Iran, Iraq, Pakistan, Peru, Syria, Tunisia, and Yemen. The countries with the most VL cases are Brazil, Ethiopia, India, Kenya, Somalia, South Sudan, and Sudan (WHO, 2010). Natural conditions such as closeness to the large rivers, seas or oceans, having active earthquake faults, and being located on high-altitude locations make these countries prone to NDs such as cyclones, floods, storms and earthquakes (Reliefweb, 2019).

Although there are several reports on the incidents of leishmaniases after NDs (fakoorziba et al., 2011; Parekh et al., 2020; Sharifi et al., 2011), the relationship between leishmaniases and NDs has not yet been

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clearly established. The published studies on ND-Leishmaniases frequency relationships are rare while there is little information on leishmaniases frequencies in the endemic regions. Moreover, the WHO datasheets are deficient on adequate leishmaniases frequencies data in the endemic countries (WHO, 2019a). Therefore, we systematically reviewed and collected all reported data on the related topics to answer whether NDs increase leishmaniases frequencies (incidence/prevalence). Since the published articles focused on the impact of NDs on leishmaniases were scarce, we searched all ND events and leishmaniases frequencies reported from countries with high incidence of leishmaniases in the last two decades in order to investigate their relationships.

2. Methods

2.1. Search strategy and selection criteria

The electronic databases including National Library of Medicine through Pubmed, Scopus, Cochrane Register, Clinical key and Google Scholar were systematically searched for the duration of January 2000 till January 2020. The countries selected for CL frequency studies were Afghanistan, Algeria, Brazil, Colombia, Iran, Iraq, Pakistan, Peru, Syria, Tunisia, and Yemen. For VL frequency, Brazil, Ethiopia, India, Kenya, Somalia, South Sudan, and Sudan were selected. These countries are almost always on the list of countries with high burden of leishmaniases (WHO, 2019b, 2019c). For each country selected, an initial keyword search was used based on Medical Subject Headings (MeSH) with several combinations of terms: “leishmaniasis” OR “cutaneous leishmaniasis” OR “visceral leishmaniasis” AND “frequency” OR “prevalence” OR “incidence” AND name of the countries. The reference lists of preliminary collected studies were also hand-searched for additional references. Furthermore, the Global Health Observatory information for VL and CL maintained by the WHO were also explored and summarized. The original articles were included if their reported data contributed to finding human VL/CL frequencies of the selected countries and their full texts were also available. Only publications in English language were included.

In studies on CL, when the total numbers of cases were not reported and instead the frequency of scars and active lesions were reported separately, the frequency of scars as final CL frequency was recorded. The following types of studies were excluded: 1- Vector or non-human hosts, 2- Ecological and immunology, pathogenesis, histopathology, or parasite species, 3- Treatment or diagnostic tests for VL or CL, 4- Mucocutaneous, post-kala-azar dermal leishmaniasis, and other forms of leishmaniases rather than VL and CL, 5- *In vitro* and *in silico* studies without any community/hospital-based data on leishmaniases frequencies, 6- Case reports and case series of less than ten patients, 7- Review articles, commentary and letters to editors without reporting any original data, 8- Self declared claims without experimental data. The articles that only reported the number of leishmaniases cases without reporting the sample size and articles without mentioning the prevalence or incidence of leishmaniases were also excluded. Moreover, studies that primarily designed to test patients with diseases other than leishmaniases (*e.g.* HIV or tissue-recipients patients) were excluded.

We conducted this systematic review based on the PRISMA guidelines (Liberati et al., 2009; Moher et al., 2009). The articles were selected using two steps evaluations. First, the titles and the abstracts of all articles were independently reviewed by two researchers (AA and MR). Second, the selected articles were reviewed for qualification by three investigators (MR, RCL and FN). The criteria for inclusion/exclusion were reported by each investigator, followed by the resolution of conflicting data through discussions.

2.2. Data extraction

Two independent readers (MR and AA) extracted the data using a pre-prepared data form which included the following information: Setting (country), the published record (year, author), the aim, the study design, and the main outcomes. The main outcomes that we looked for were the frequency (prevalence/incidence) of VL or CL in the community or among the patients referred to health facilities. The CASP checklist (for reporting epidemiological studies) was used to assess the critical appraisals of the studies.

2.3. ND data

The present study only focused on climate-related and geophysical NDs including floods, flash floods, hurricanes, cyclones, storms, earthquakes, tornadoes, tsunamis, landslides, volcanic activities, wildfires and droughts. The list of main ND events of each country was obtained from reliefweb ⟨https://reliefweb.int/disasters⟩ and centre for Research on the Epidemiology of Disasters (CRED) ⟨https://www.cred.be/⟩ databases. All ND reports from January 2000 till January 2020 were found and their types, affected areas, the centers, and the occurring times were recorded for further analysis. Non-natural disasters such as technological disasters, epidemic diseases, and insect infestations were excluded. All maps were created using Datawrapper version 1.25.0 ⟨https://www.datawrapper.de/⟩.

2.4. Final selection

To find a relationship between NDs and the leishmaniases frequencies, only articles that reported the frequency data of the exact or affected region by ND, were included. All leishmaniases frequencies reports before a ND were recorded as “before ND data” and all reports between 0 and 3 years after a ND, were recorded as “after ND data”. To select a report, no other NDs should had happened at that region during that time frame. If there were several NDs in a specific region in sequential years, all the related articles to that region in that particular time were excluded. In summary, the best pattern that we looked for was as depicted in Fig 1.

2.5. Data analysis

The frequency (prevalence/incidence) of leishmaniases for each study was assessed separately. Data were analyzed by the leishmaniasis type, region, and the leishmaniasis frequency-ND relationship. In order to find this relationship, the data of each study were grouped into before ND and after ND (in year) and the differences in their leishmaniases frequencies were analyzed. Meta-analysis with random effect approach was performed to calculate the frequency of leishmaniasis before and after a ND. For this end, ITSA (Interrupted Time Series Analysis) package, known as quasi-experimental time series analysis, was used to assess the effects of a ND on frequency of leishmaniasis. Analyses were done at 95% confidence level by using STATA software version 14 (STATA Corp, College Station, TX, USA). P value ≤ 0.05 was considered statistically significant.

3. Results

3.1. Search results

Eleven countries with the most CL cases and seven countries with the most VL cases were analyzed as mentioned above. The selected countries for VL studies were located in South Asia (India), Africa (Ethiopia, Kenya, Somalia, South Sudan, and Sudan), and South America (Brazil) (Fig. 2). Since few studies have intended to find ND-leishmaniases relationships, we had to find all major NDs and reported CL/VL cases in these countries and verify the presence of a possible relationship between them. For this goal, we carefully reviewed all the related articles found and those which met the inclusion criteria were selected using the selection process, the screening strategy and the exclusion reasons that are presented in Fig. 3. The details of the NDs and the leishmaniases

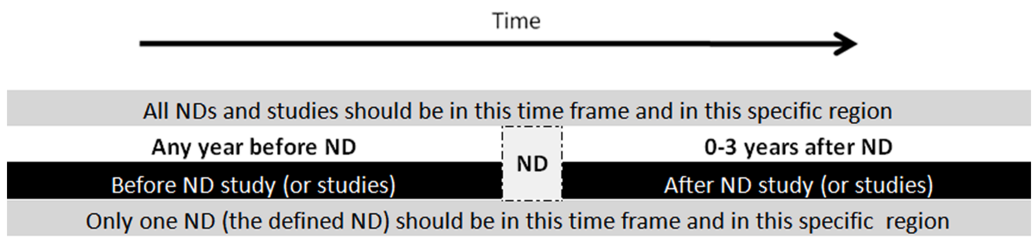

Fig. 1. The designed pattern to select studies on ND-leishmaniases relationships. The best studies we looked for were those done in one specified region at the time frames that only one ND had happened and both the frequency of leishmaniasis before the ND and 0–3 years after it had been described.

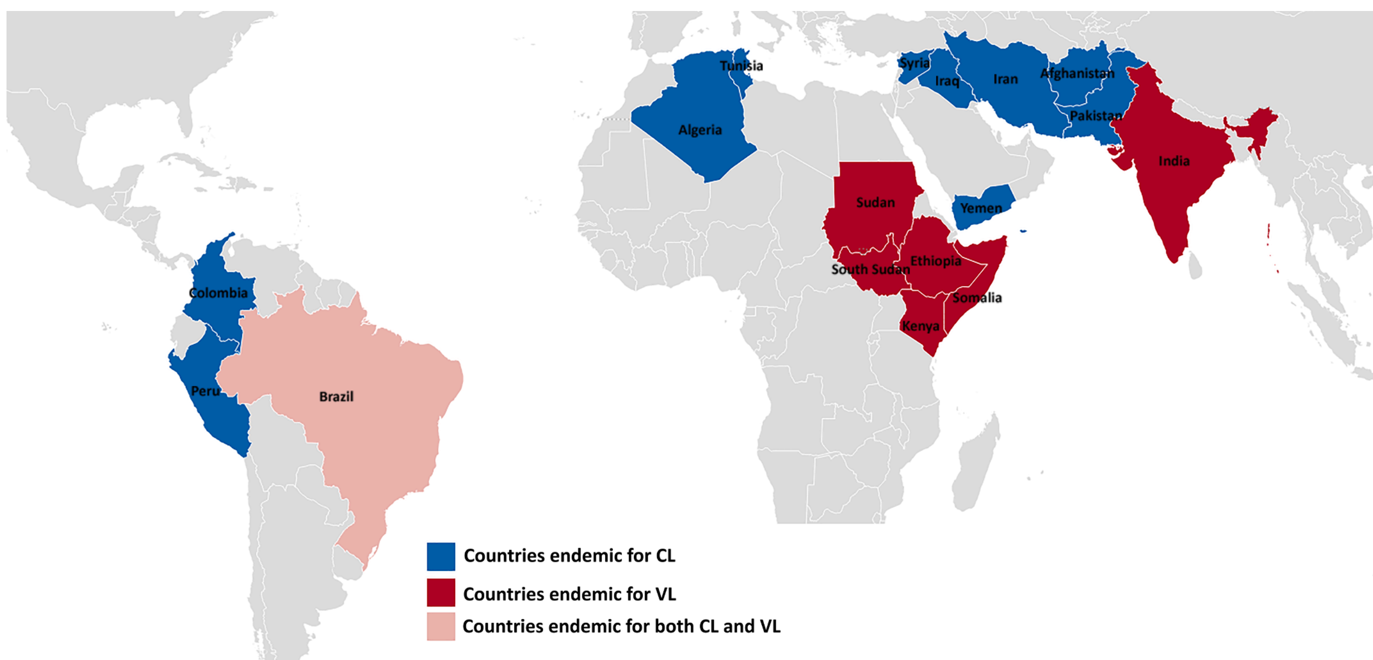

Fig. 2. The selected countries for leishmaniasis. Seventeen endemic countries for CL or VL were selected, located in South Asia, the Middle East, Africa, and South America. It is noteworthy that a few CL endemic countries have also VL endemic regions and *vice versa*. In our study, countries were classified based on having the most endemic regions for a particular type of leishmaniasis, according to the WHO reports.

reported for each country are presented in Tables S1 and S2. In total, 39 studies were included in this research, which their key information are reported in Table S3.

3.2. Description of ND-CL relationship in the included studies

Fourteen studies for evaluation of ND-CL relationship (eleven from Iran and three from Pakistan) were finally selected. The included studies in Iran were from eight regions, namely Ilam, Kerman, Fars, Khuzestan and Bushehr provinces, as well as Bam, Darab, and Zarindasht cities (Fig. 4). These regions are considered endemic for CL (Norouzinezhad et al., 2016) and are also prone to NDs such as earthquakes (Fig. 4). Only two studies intended to find a relationship between a ND and CL frequency in Bam city where a devastating earthquake occurred in 2003 (fakoorziba et al., 2011; Sharifi et al., 2011). Other nine studies investigated CL frequency without considering any potential ND effects. In order to find any changes in CL frequency after NDs, studies that conformed to our designed pattern (Fig. 1) were selected. Only four studies had these criteria and were used for meta-analysis. These articles reported the CL frequency data of Bam city, Zarindasht city and Bushehr province in Iran (Aflatoonian et al., 2014; fakoorziba et al., 2011; Norouzinezhad et al., 2016; Sharifi et al., 2011). All three studies of Pakistan have been done in Khyber Pakhtunkhwa (Fig. 4). There are many CL cases in this region (Ahmad et al., 2013; Hussain et al., 2017) with approximately 15 NDs since 2000 (Fig. 4). All three studies in this region were carefully reviewed for possible adjustments with our designed pattern (Fig. 1); however, none of them met the full criteria and were excluded from further analysis.

3.3. Description of ND-VL relationship

After the eligibility steps, 25 studies that possibly showed ND-VL relationship were remained. Among these studies, 16 were from Brazil, six were from Ethiopia, and three were from Sudan. The Brazilian studies reported VL cases from 10 regions, namely Mato Grosso, Rio Grande do Norte, Minas Gerais, Maranhão, Sergipe, Bahia, Pernambuco, Ceará, Piauı, and Tocantins states (Fig. 5)(Dantas-Torres, 2006). Twenty-eight NDs have occurred in these regions since 2000 (Fig. 5). All these studies intended to find VL frequencies without considering any potential ND effects. Therefore, we found all NDs reported in these regions within the affected areas and tried to find any changes in VL frequencies after the NDs. To do so, based on the above-mentioned designed pattern (Fig. 1), only 5 studies were compatible which were used for meta-analysis. These articles reported the VL frequencies data from Mato Grosso, Rio Grande do Norte, Minas Gerais, and Sergipe states (Brito et al., 2014; Bruhn et al., 2018; Campos et al., 2017; Lima et al., 2012; Ursine et al., 2016).

The Ethiopian studies were from Libo Kemkem (two studies),

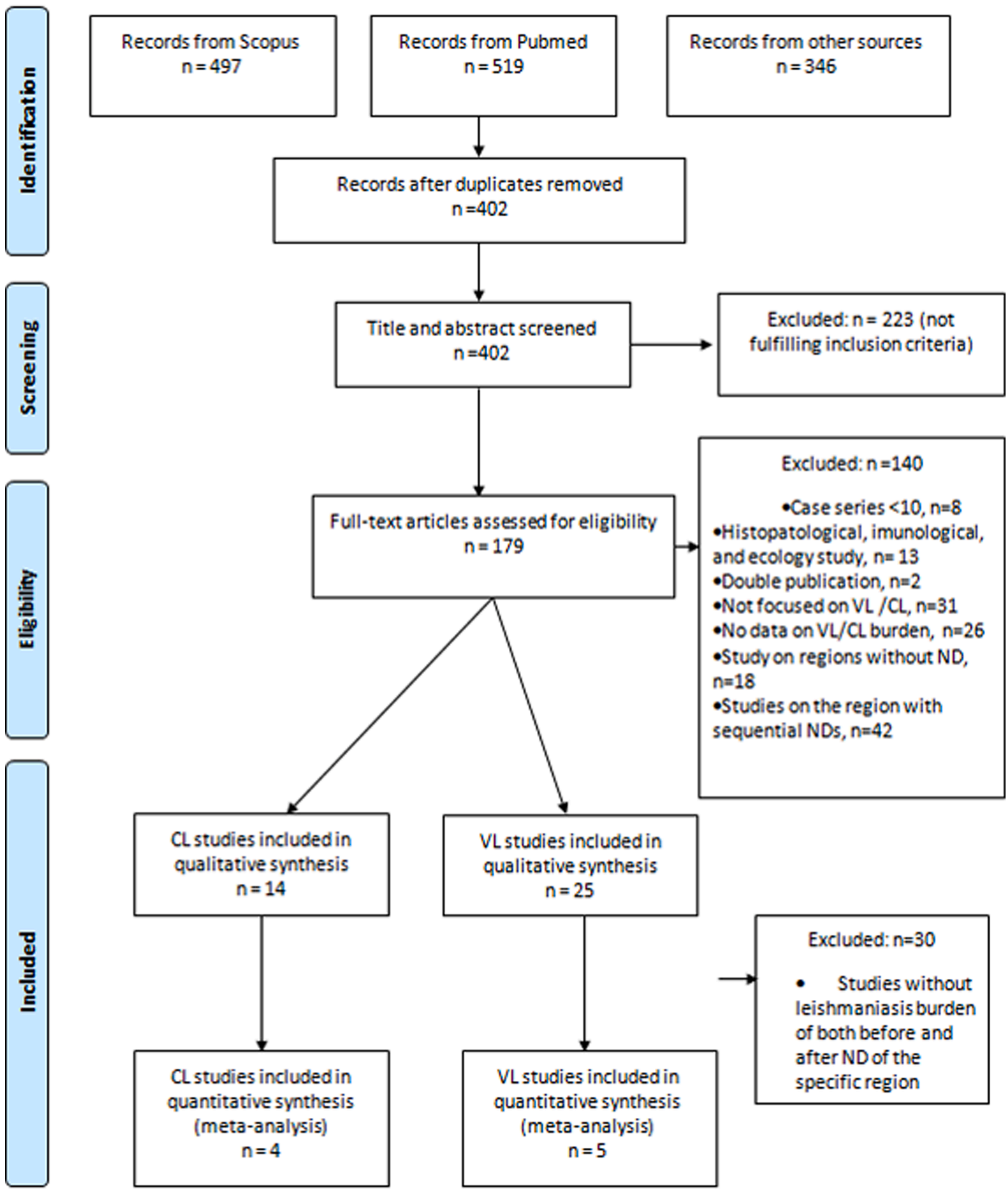

Fig. 3. The PRISMA flow diagram.

Armachiho (two studies), Kafta-Humera (one study), and Tigray-Welkait (one study) in the northern parts of the country (Fig. 5). Many VL cases in these regions have been reported (Alvar et al., 2007; Aschale et al., 2019; Ayehu et al., 2018; Lemma et al., 2015; Sordo et al., 2012) while 15 NDs have also been occurred in these regions since 2000 (Fig. 5). All these studies were carefully reviewed for possible adjustments with our designed pattern. Consequently, none of them met the full criteria and were excluded from further analysis. Moreover, all three studies of Sudan have been done in Gedaref state (Fig. 5). There have been many VL cases in this region (el-Safi et al., 2004; Elnaiem et al., 2003; Mohamed et al., 2019) which had been prone to approximately 15 NDs since 2000 (Fig. 5). After careful reviewing of all these studies for possible adjustments with our designed pattern, none were found to meet the full criteria and hence were excluded from further analysis.

3.4. Meta-analyses of ND-leishmaniases frequencies relationships

The meta-analyses consisted of four studies for CL-ND and five studies for VL-ND relationships. These studies contained leishmaniases incidences of the specified regions before and after a ND (Table 1). Meta-analyses were carried out using the leishmaniasis incidence (*i.e.* positive cases per 100,000 populations). As shown in Fig. 6, the incidence rate of

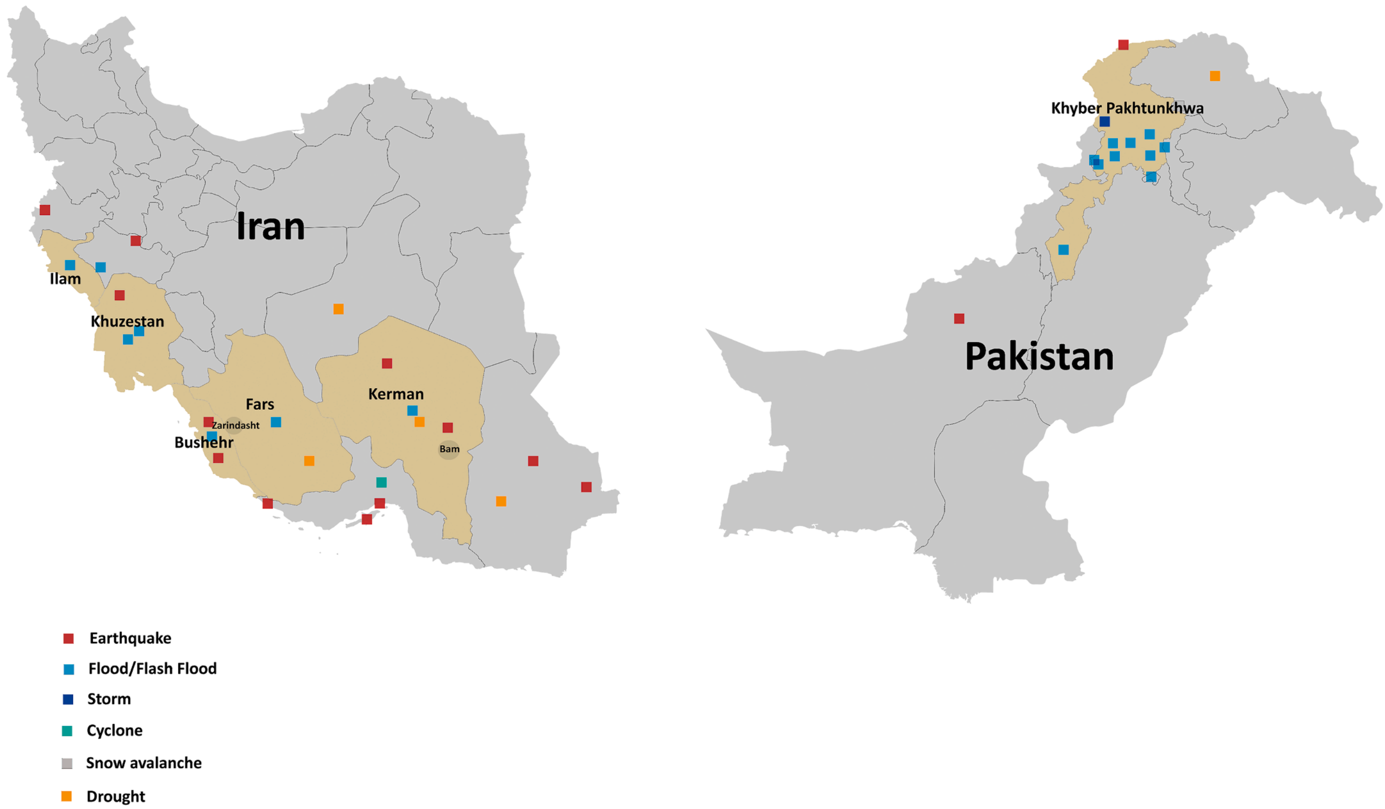

Fig. 4. The regions included for CL studies. Fourteen studies (11 in Iran and three in Pakistan) were selected to find ND-CL relationship. The regions with the major NDs since 2000 have been shown on the map. Only major NDs which had affected the specified regions (not the whole country) have been shown. Note: Some NDs (*e.g.* storms, floods and droughts) affect wider places; however to simplify the figure, only the most-affected regions are shown.

Fig. 5. The regions included in our VL studies. After eligibility steps, 25 studies (16 in Brazil, six in Ethiopia and three in Sudan) that might show a ND-VL relationship were remained. The regions of these studies and the major NDs happened since 2000 are shown on the map. Only major NDs affected the specified regions (not the whole country) are shown. Note: Some NDs (*e.g.* storms, floods and droughts) affect wider places; however to simplify the figure, only the most-affected regions are shown.

CL in specified regions was increased after the NDs, although the difference was not statistically significant (P value = 0.065). The incidence rate of VL was increased after the NDs (Fig. 7). In fact, the rate of incidence was low before the ND while the incidence rate was increased after the ND and maintained high for several years later.

4. Discussion

In the present study, the effects of NDs on CL and VL frequencies in 17 endemic countries were investigated. The country investigated in South Asia was India which is a LMIC country. The northern parts of India (especially Bihar state) are endemic for VL with an incidence rate of 6.2 cases/100,000 population (WHO, 2015a). Various NDs such as floods, landslides, earthquakes, cold waves, tropical cyclones, and severe local storms take place in India and especially in VL-endemic areas, annually (Reliefweb, 2019). These NDs cause displacements of the residents and may expose the populations to sandflies which carry *Leishmania* parasites, leading to increased VL incidences. The Middle Eastern

Table 1
The leishmaniasis incidence (cases number per 100,000 population) of final included studies.

Disease type	Studies	Place	Years before ND 7–8 yr	6–7 yr	5–6 yr	4–5 yr	3–4 yr	2–3 yr	1–2 yr	0–1 yr	ND	Years after ND 0–1 yr	1–2 yr	2–3 yr	3–4 yr	4–5 yr	5–6 yr	6–7 yr	7–8 yr
Cutaneus leishmaniasis	Sharifi-2011-a	Bam	–	–	–	–	150	250	125	75		200	650	1200	900	875	–	–	–
	Aflatoonian-2014		–	–	–	–	–	–	–	–		700	1600	5100	4600	3600	3200	2500	–
	Fakoorziba-2011	Zarindasht	–	–	–	–	–	–	–	58.6		491	864	–	–	–	–	–	–
	Norouzinezhad-2016	Bushehr province	–	–	–	–	–	–	14.5	10.9		11.1	–	–	–	–	–	–	–
Visceral leishmaniasis	Brito-2014	Mato Grosso (Jaciara city)	11.8	15.5	3.7	0	0	11.6	0	0		11.6	19.3	–	–	–	–	–	–
	Lima-2012	Rio Grande do Norte (whole state)	45	22	15	7	8	5	7	8		12	10	5	–	–	–	–	–
		Rio Grande do Norte (Parnamirim city)	19	6.2	5	4.9	2.5	1.25	1	1		1	1	0.5	–	–	–	–	–
	Bruhn-2018	Minas Gerais (Belo Horizonte city)	–	–	–	–	–	–	2	1.5		4.5	6.3	5.5	5	3.5	2	1.5	–
	Ursine-2016	Minas Gerais (Araçuaí city)	–	–	–	–	–	–	19.4	19.3		16.6	8.3	8.3	16.7	19.4	19.4	19.3	–
	Campos-2017	Sergipe (whole state)	–	–	–	–	–	–	3.1	3.4		5	3.9	5.1	5	6.8	3.1	3.4	–
		Sergipe (Aracaju city)	–	–	–	–	–	–	2.1	2.2		3	2.3	2.5	3.2	4	2.1	2.2	–

The numbers show the leishmaniasis incidence (cases number per 100,000 population).
Yr = year.

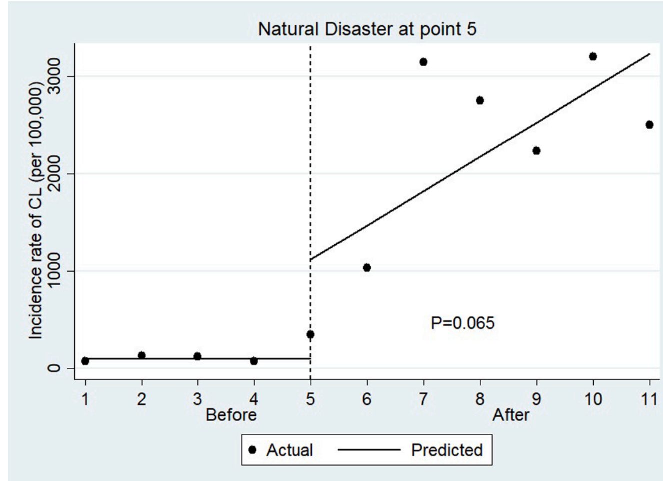

Fig. 6. The effects of NDs on CL incidence. The incidences of CL in 0–4 years before a ND was low while it increased gradually 0–7 years after a ND. The dots are actual incidence numbers reported in the studies while the line is a predicted trend of our data, generated by our statistical method.

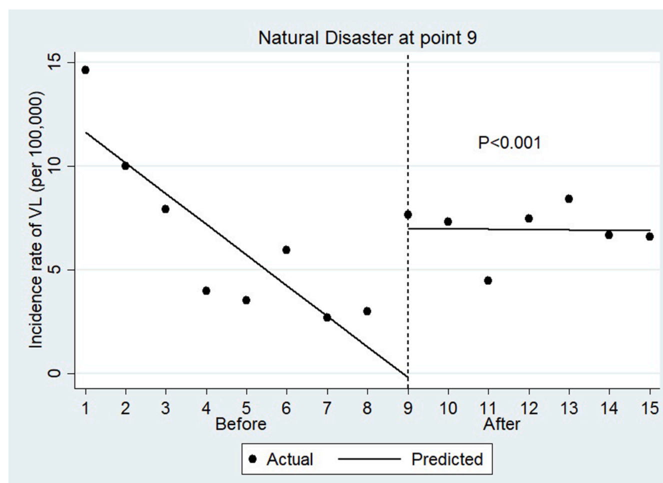

Fig. 7. The effects of NDs on VL incidence. The incidence of VL in 0–7 years before a ND was decreasing while it increased and maintained for 0–7 years after a ND. The dots are actual incidence numbers reported in the studies while the line is a predicted trend of our data, generated by our statistical method.

countries studied here were Afghanistan, Pakistan, Iran, Iraq, Yemen, and Syria. The populations in these mostly LMIC have been confronted with various NDs such as earthquakes, droughts, cyclones, floods, and landslides (Reliefweb, 2019) as well as geopolitical problems such long lasting wars or civil wars. Both types of Zoonotic and Anthroponotic CL which are endemic in these countries (WHO, 2010) are spreading to new areas due to mass migrations and the lack of appropriate prevention, control and treatment measures (Burza et al., 2018). Although the overall incidence rate of CL in some countries can be found in the WHO annual reports, there is no accurate data on local or regional CL frequencies. Since 2000, the numbers of new CL cases in few of these countries have been fluctuated through different years while this rate has been constant for others (Salam et al., 2014). The reason of these variations or unchanged rate of CL incidence is unknown and needs more studies. It should be noted that although there are a few VL endemic regions in Iran (especially areas inside the northwestern provinces), the whole country is not considered as VL endemic (Rostamian et al., 2021). Therefore, in the present study, Iran was assumed as a

CL endemic country only.

The African countries studied here were Algeria, Tunisia, Sudan, South Sudan, Somalia, Kenya, and Ethiopia. They are basically developing countries with various socioeconomic problems and in some cases have long suffered from neglected medical infrastructures (Oleribe et al., 2019). Algeria and Tunisia are endemic for CL while the other four countries are endemic for VL (Aoun and Bouratbine, 2014; Burki, 2009). In Algeria and Tunisia, the highest CL incidence rates were reported in 2005 and then the rates decreased and reached to a stable level due to unknown (or unpublished) reasons. Furthermore, in VL endemic countries, the new cases are fluctuating up and down through different years, without known (or published) reasons (WHO, 2019d). Most importantly, a VL outbreak was reported in northern parts of South Sudan in 2014 which has been considered as a disaster (WHO, 2019d). The African countries are also prone to different types of natural disasters including droughts, floods, earthquakes and locust infestations (Reliefweb, 2019). These disasters may change the whole ecosystems and lower the hygiene levels to the critical conditions which increase the risk of many diseases including leishmaniases.

The South American countries investigated here were Brazil, Colombia and Peru that are upper middle income countries with several CL endemic regions. The CL incidence rates have been reported as 18, 34, and 23 cases/100,000 population in the endemic areas of Brazil, Colombia, and Peru, respectively (WHO, 2015b, 2015c, 2015d). Brazil is also endemic for VL with an incidence rate of approximately 4 cases/100,000 population in the endemic areas of the country. Since 2000, the numbers of both CL and VL new cases have slightly decreased in Brazil while in the other two countries, the rate of new CL cases has remained unchanged (WHO, 2015b, 2015c, 2015d). Annually, South American countries are affected by various NDs such as floods, droughts, wildfires, and earthquakes. Due to the heavy rainfalls in Amazon region, the most frequent NDs in these countries are floods which have a devastating effect on the ecosystem and provide a suitable environment for fertilization of *Leishmania*-carrying sandflies (Reliefweb, 2019).

Although our results generally point to the fact that incidence rates of leishmaniases increase after NDs, there are four main limitations in this study which should be considered. First, the available data used for these studies were not robust enough to undoubtedly find a leishmaniasis-ND relationship. Second, all studies performed on leishmaniases frequencies are dispersed in different areas of the endemic countries which make them difficult to be merged in order to establish a solid leishmaniasis-ND relationship. Additionally, disease control programs in the countries studied have been updated with time, and in some countries the reporting of leishmaniasis cases has not always been mandatory. This has led to the more limitations to conduct research such as our study. Third, in the aftermath of NDs, the medical care services usually focus on more urgent conditions and diseases, and often neglect the diseases such as leishmaniases which are normally non-fatal. This issue is another source of underreported cases and lack of records. Fourth, considering the effects of NDs and their major consequences in the developing countries that do not necessarily report and publish in English, the choice of language (*i.e.* English studies only) is another limitation of the present study.

Nevertheless, based on our findings and to avoid detrimental consequences, we suggest that guidelines regarding leishmaniases risk control after NDs be prepared in the endemic countries. These guidelines should include the practical guidelines such as how to use bed netting to avoid sandflies bites, how to make temporary safe shelters, how to educate the affected populations and how to medically treat the infected population, to name a few. Proper surveillance systems that detect and record all leishmaniases cases will definitely contribute to better evaluation of leishmaniasis-ND relationship in the future.

Moreover, it should be noted that in spite of NDs, which cause accidental and usually short-term environmental changes, long-term changes such as climate change may also have impact on the distribution of leishmaniases. Climate change is defined as a long-term change in the average weather patterns due to several phenomena such as global warming. Climate change may directly alter the parasite development and the vector competence through changes in temperature or it may indirectly impact on the spreading, abundance and range of the reservoirs and the vectors. Furthermore, the distribution of leishmaniases could be modified through socioeconomic changes made by climate change which in turn impact on a population's exposure to the reservoirs and the vectors (Ready, 2008). Research have reported the effects of climate change on leishmaniases (Booth, 2018); however, similar to facts mentioned about the ND effects on leishmaniases, further studies are needed to clarify the effects of climate change on leishmaniases incidence.

Altogether, in our attempt to find a possible relationship between NDs and changes in leishmaniases frequencies around the world, we came to this conclusion that there is a big knowledge gap on this topic. Although we found nine articles that were compatible with our defined pattern of finding ND-Leishmaniases relationships, only two of them had directly investigated the ND (earthquake) effects on CL. Furthermore, these two studies had been done on the same ND (*i.e.* Bam earthquake in 2003) by the same research groups that could have publication bias (fakoorziba et al., 2011; Sharifi et al., 2011). Therefore, we acknowledge that the effects of NDs on leishmaniases require more meticulous and comprehensive investigations.

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CRediT authorship contribution statement

Mosayeb Rostamian: Conceptualization, Data curation, Formal analysis, Methodology, Software, Project administration, Writing - original draft, Writing - review & editing. **Shahab Rezaeian:** Data curation, Formal analysis, Writing - review & editing. **Mohamed Hamidouche:** Investigation, Validation, Writing - original draft. **Fariborz Bahrami:** Validation, Writing - original draft, Writing - review & editing. **Keyghobad Ghadiri:** Funding acquisition, Resources. **Roya Chegeneh Lorestani:** Data curation, Investigation. **Fatemeh Nemati Zargaran:** Data curation, Investigation. **Alisha Akya:** Project administration, Supervision, Validation, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

None declared.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.actatropica.2021.105855.

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