





Real-time impact of COVID-19 pandemic on cutaneous leishmaniasis case finding and strategic planning, preventive interventions, control and epidemiology in a region with a high burden of cutaneous leishmaniasis and COVID-19: A cross-sectional descriptive study based on registry data in Ilam-Iran

Morteza Shams¹ | Ayoub Rashidi^{1,2} | Jasem Mohamadi^{1,3} | Mohamad Moradi^{1,3} |
 Reza Pakzad¹ | Razi Naserifar¹  | Jahangir Abdi¹ | Fariba Ghelichi¹ |
 Arezoo Bozorgomid⁴ | Nahid Maspi¹ | Azra Kenarkoohi⁵  | Yasin Mohammadi⁶ |
 Amir Abdoli⁷  | Shahab Falahi¹ 

¹Zoonotic Diseases Research Center, Ilam University of Medical Sciences, Ilam, Iran

²Public Health Staff, Infectious Diseases Control Unit, Ilam University of Medical Sciences, Ilam, Iran

³Department of Pediatrics, School of Medicine, Emam Khomeini Hospital, Ilam University of Medical sciences, Ilam, Iran

⁴Infectious Diseases Research Center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran

⁵Department of Microbiology, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran

⁶Medicine Faculty, Kateb University, Kabul, Afghanistan

⁷Zoonoses Research Center, Jahrom University of Medical Sciences, Jahrom, Iran

Correspondence

Shahab Falahi, Zoonotic Diseases Research Center, Ilam University of Medical Sciences, Ilam, Iran.

Email: shahabivan@gmail.com

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Abstract

Background and Aims: Cutaneous leishmaniasis (CL) is a severe parasitic disease affecting people, mostly in underdeveloped nations. As a zoonotic infection yearly incidence of CL depends on several parameters such as demographic, epidemiological, and environmental factors as well as prevention and control measures. The sudden outbreak of pandemics such as SARS-Corona-Virus-2 pandemic, can probably affect the incidence or reporting of other diseases, especially infectious diseases, in various ways such as pressure on health systems, providing sanitary services and its components, lockdowns and changes in people's living habits.

Aim: This study aimed to evaluate the COVID-19 impact on the incidence and other epidemiological aspects as well as control measures of CL in Ilam Province-Iran.

Methods: Required data was extracted from the CL registration system in Ilam from 2014 to 2021 to demonstrate the trend of CL incidence before and after COVID-19 pandemic.

Results: Based on our results, a declining pattern of CL incidence was observed, accompanied by the advent and intensification of the viral pandemic in Iran and Ilam province. Although, this decreasing pattern was not integral in all areas, and even increase in CL detection was emphasized in some regions.

Conclusion: It may be inferred that the COVID-19 pandemic may disrupt treatment programs of CL cases, rodent nest destruction, and fighting vector insects.

KEYWORDS

case finding, COVID-19, cutaneous leishmaniasis, epidemiology, high, impact, pandemic

1 | INTRODUCTION

Cutaneous leishmaniasis (CL) is a well-known vector-borne parasitic disease with Phlebotomine sand flies as the primary biological vector.^{1–4} The disease imposes a substantial public health burden, particularly in developing countries of Asia (Iran, Syria, Afghanistan, and Saudi Arabia), Africa (Algeria), and South America (Peru and Brazil).^{2,5–8} The Old World CL, including in Iran, usually represents two forms: (i) urban CL characterized by dry lesions caused by *Leishmania tropica* and (ii) rural CL causing wet lesions rendered by *L. major*.^{9–11} The implication of standardized CL diagnosis has led to the established networks of laboratories at three levels, including health centers, academic reference laboratories, and national reference laboratories. Reportedly, most experiments are performed in the academic reference laboratory and at health centers in 31 Iran provinces.^{8,9,12,13}

The coronavirus disease 2019 (COVID-19) pandemic has inevitably caused several substantial health conflicts in many countries throughout the globe.^{14–21} The first COVID-19 case in Iran and Ilam province was detected on Wednesday, 2020-2-19 and Saturday, 2020-2-29, respectively, followed by an absolute lockdown of educational and academic institutions and many other occupations across the country to minimize the risk of viral transmission. Consequently, preventive measures and control programs for infectious diseases were interrupted, including national Leishmaniasis control efforts.^{22–25} At a global scale, affected countries maximized health care services to decrease the chance of transmission, while they should confront the exponentially increasing number of COVID-19 patients as a significant challenge.^{26–30}

Neglected tropical diseases (NTDs) are a diverse group of communicable diseases affecting 149 countries and billions of people in tropical areas. The NTDs have received much attention and investment in recent years to reduce the burden; however, they still cause productivity loss and disability-adjusted life years. This integrated approach to NTD control is now recognized as an essential and vital global public health solution.^{31–33} The health impact of the COVID-19 pandemic is likely to be much more severe and prolonged in those countries affected by NTDs.^{16,17,19,29,34,35} Nevertheless, the effect of anti-COVID-19 measures performed in primary healthcare stations should be emphasized in detecting chronic parasitic infections, mainly in those regions where several NTDs co-existed.^{29,36,37} For some NTDs, delays in active case detection will increase the incidence of new infections.³⁸

During the COVID-19 pandemic, coexistence with other diseases is not unusual, and misdiagnoses may be inevitable. Similarities in the febrile course and other manifestations of some diseases may lead to clinical misdiagnosis of COVID-19 infection, which can further complicate the clinical picture and result in misdiagnosis.³⁹

In Iran, the prevalence of parasitic infection was reported between 4.7% and 56%. This issue has been significantly observed in regions with low socioeconomic status, limited sanitation, and geographic factors such as location, physical features, natural distribution, and so on.^{40–47}

Iran is one of the regions severely affected by the current pandemic, and the emergence of COVID-19 has had a significant

impact on the burden of communicable and non-communicable diseases worldwide as well as in Iran.^{15–17,19,20,28,35,37,48–56}

Many infectious diseases directly or indirectly impact each other and can impact clinical features or epidemiological picture of another infection.^{16,24,50–52} The World Health Organization (WHO) published a guideline on maintaining essential healthcare services during the viral pandemic.⁵⁷ However, it is not entirely possible to evaluate the true impact of COVID-19 on the global burden, detection strategies, and control measures of several parasitic diseases, but the negative consequences will undoubtedly be profound.^{58–60} Being reported in 98 endemic countries and considered a public health risk for over 350 million people worldwide, CL is also a severe parasitic infection in Iran, with about 20,000 new cases annually. It is frequently reported in Isfahan, North Khorasan, Kerman, Khuzestan, Fars, and Ilam provinces. Ilam, primarily children, are more prone to CL due to the abundance of rodent reservoirs and biological vectors, with Dehloran, Mehran, and Abadan as critical hotspots for CL transmission.

The health system of Iran was severely affected by the COVID-19 pandemic, and most budgets were assigned to COVID-19 management. In Ilam province, the routine rodent control program, the retraining courses for health personnel, and the implementation of health education programs for inhabitants of endemic regions during the first year of the COVID-19 pandemic entirely ceased.^{56,61–66}

Based on our knowledge to date, the studies on the effect of the COVID-19 pandemic on Leishmaniasis status performed at countries or higher levels, and there is almost no study fully discussing the impact of COVID-19 on CL control programs at a provincial level, even though these impacts may vary greatly depending on the severity of local COVID-19 or CL epidemic.

Moreover, some preventive measures of zoonotic and vector-borne diseases, such as case finding and screening and rodent control programs, as well as treatment follow-up, were interrupted during the COVID-19 pandemic in Iran and other parts of globe, especially during 2020–2021^{22–25}; that led us to check for probable impacts of COVID-19 pandemic occurrence on trend and other possible features of CL in Ilam province as one of the most important hotspot of CL that interestingly was under severe attack of COVID-19.

Based on our search, a detailed investigation of the COVID-19 pandemic effects on the burden of CL in endemic areas had not been performed. Herein, we assessed the impact of COVID-19 and its preventive strategies on the incidence, distribution, and other epidemiological aspects of CL in Ilam province, west of Iran, as a region with a high burden of COVID-19 and CL cases.

2 | METHODS

Today, different types of models and analyzes are used to investigate different aspects of infectious diseases and can provide high benefits at low cost.^{37,67} The present study aimed to demonstrate the possible impacts of the COVID-19 pandemic and related strategies on CL epidemiology, prevention, and control.

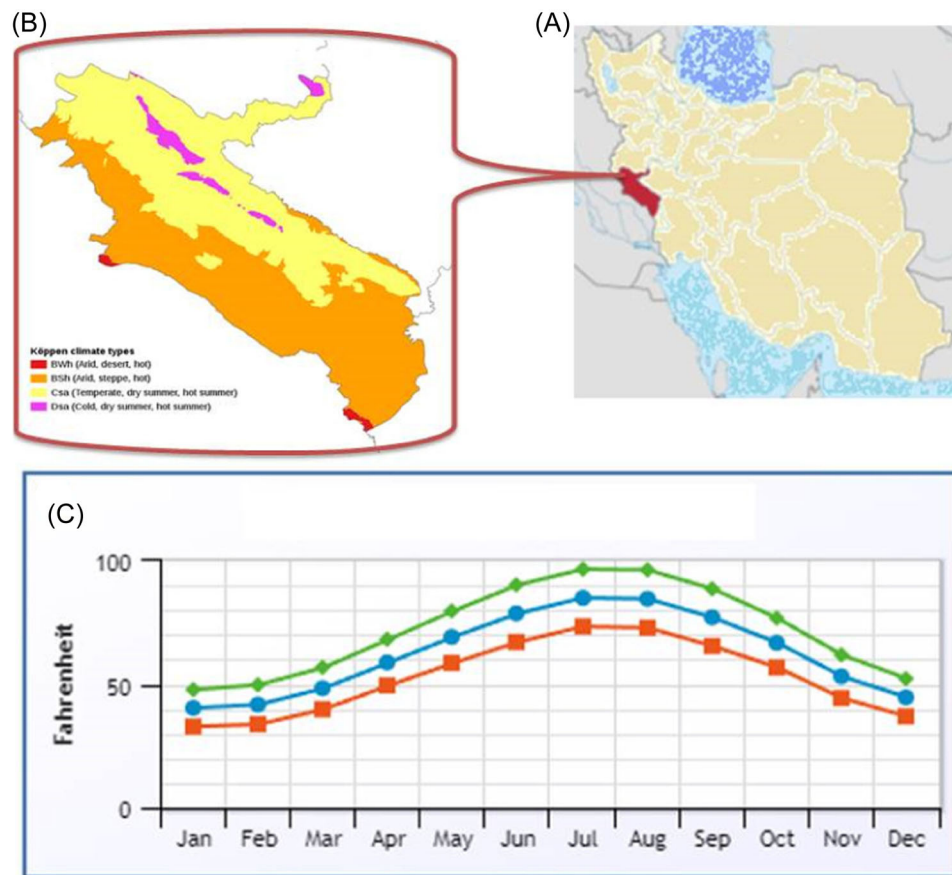


FIGURE 1 (A) Geographic location, (B) average temperature,⁶⁸ and (C) Koppen climate types (full-size image at Appendix: Figure A1)⁶⁹ of the Ilam province in Iran.

2.1 | Study settings

The Ilam Province is located in the southwest of Iran with a total area of 20,150 km² (7780 sq mi) and is bordered by Iraq to the west (Figure 1). By the end of 2019, the resident population was 580,158 individuals, of which 295,199 and 284,959 were men and women, respectively. In total, 159,310 families are residents in Ilam province. The population density in 2016 was 28.8 people/km². The urban population of this province is 395,263 people, which covers 13.68% of the province. Notably, Ilam province is the least populated province in Iran. Of the total area of Ilam province, more than 6420 km² is forest. The province's highest point is 3062 m above sea level, and the city's is 196 m above sea level. According to the provincial meteorological station statistics, January is the coldest, and July is the warmest month. The temperature of the stations has been rising from April to July and then gradually decreasing. Ilam province is neighboring Iraq and has about 435 km of the common border (the longest border) with this country.

On February 29, 2020, the first case of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was confirmed in Ilam province. The Ministry of Health in Iran launched a set of preventive protocols and interventions for all academic and nonacademic occupations to lower the risk of transmission to individuals. Since then, until December 31, 2021, 67,068 confirmed

cases and 11,740 death cases due to COVID-19 were detected in Ilam province.

2.2 | Data collection

In Iran, CL is a reportable infectious disease; hence all disease reports accompanied by required data are registered and managed through the Information Registration System of the Centre for Communicable Diseases Control, Ministry of Health and Medical Education, Tehran, Iran. We examined the impact of the COVID-19 epidemic on active and passive CL case finding and CL preventive interventions using the confirmed data stored in the province Registration System (Figures 2 and 3).

2.3 | Statistical analysis

Recorded data associated with CL cases in Ilam province were subjected to statistical analysis using Statistical Package for Social Sciences v25 (SPSS, IBM Corp). Moreover, the Cochran–Armitage χ^2 test for linear trends was utilized for trend analysis at a significant $p < 0.05$. Data were presented as numbers with percentages.

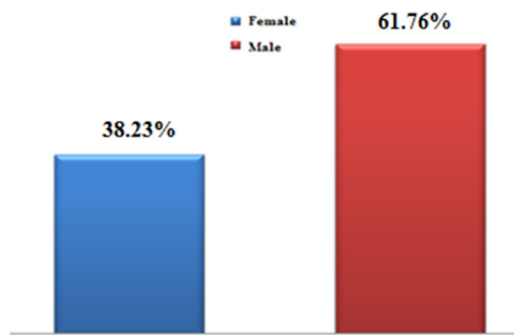


FIGURE 2 Prevalence of Leishmaniasis based on patients' sex ($p < 0.05$).

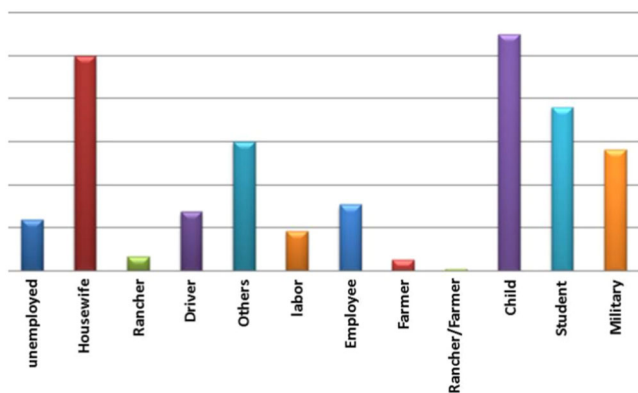


FIGURE 3 Prevalence of Leishmaniasis based on occupation ($p < 0.05$).

Categorical variables were compared using the χ^2 test for trend to evaluate the seasonal trends of each variable at the national level and in the pre-specified regions. All tests were two-tailed, and $p < 0.05$ indicated statistical significance. Finally, possible changes in the number of reported cases before and after COVID-19 onset were evaluated. Considering that our source of information was the registry and administrative system of the provincial health department during the COVID-19 pandemic, information or reporting bias may occur due to the pressure of the pandemic. Generally, to avoid any biases, in studies like our present case, we recommend that the local and native conditions and parameters related to the degree of endemicity of the infection and the conditions specified for the investigated region must be considered in the measurements.

Also, we tried to have the least amount of missed data by comprehensively examining the different information sources and checking various departments involved in the COVID-19 pandemic management and the treatment and prevention of zoonotic Leishmania infection as much as possible.

2.4 | Ethical considerations

The study was determined to be a nonresearch program evaluation. As it required no direct contact with human subjects (no interview or

sample collection, without the use of personal data) and only identified pooled program data in the context of the registry program were used, informed consent was not necessary. The project was approved by the ethical principles and the national standards for conducting Medical Research in Iran (IR.MEDILAM.REC.1398.057).

All authors have read and approved the final version of the manuscript and corresponding author had full access to all of the data in this study and took complete responsibility for the integrity of the data and the accuracy of the data analysis.

The corresponding author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

3 | RESULTS

As shown in Figures 2–5, the incidence rate of CL cases showed differences among cities of Ilam province based on various epidemiological variables. The incidence rate per 100,000 individuals was 322.1, 258.1, 233.5, and 168.6 in men from 2014 to 2017, while it was demonstrated to be 213.2, 189.1, 138.1, and 96.8 in women. Generally, men (61.7%) are more infected than women (38.23%; $p < 0.05$). Reportedly, Malekshahi, Mehran, and Dehloran had the highest incidence of CL, while the highest number of cases were reported in 2014. It was inferred that the number of CL cases gradually decreased within the study period (Figure 3). Our findings showed that Ilam province has the highest incidence of CL in Iran (from 69.7 to 155 per 100,000 people in different cities of the province). In general, the pattern of national and provincial occurrence and the ratio of gender distribution in the province has not changed significantly during the pandemic. This probably is due to differences in the prevalence of COVID-19 or differences in epidemiological, environmental, ecological, and some other related factors between the province's cities. In terms of occupations, housewives, students, children, and military personnel were mainly affected.

During 2014–2021, a decreasing trend in CL incidence was observed in Ilam province, with an absolute decrease in 2020, which coincided with the arrival and intensification of the coronavirus pandemic in Iran and the Ilam province. However, this declining pattern had no required distribution across the province, and even there was an increase in CL detection in some areas (Figure 4).

Another finding of this study was that most cases were found in urban, rural, and nomadic regions, respectively, while some cases did not belong to the above classification; however, the CL trend was not significantly different before and after the pandemic (Figure 5). The number of lesions per individual ranged from 1 to 30, while most cases suffered from only one to two lesions. In most cases, systemic or topical Glucantim, glucantim combined with cryotherapy of lesions, and cryotherapy alone were the most prominent therapeutic approaches. Dehloran and Mehran showed the highest level of infection, respectively.

FIGURE 4 Trend of CL from 2010 to 2021 ($p < 0.05$). CL, cutaneous leishmaniasis.

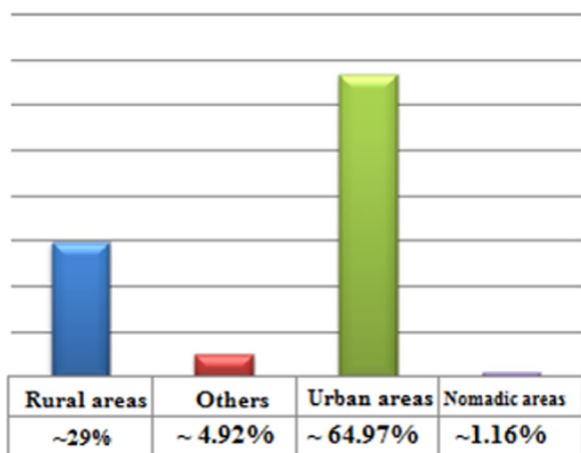
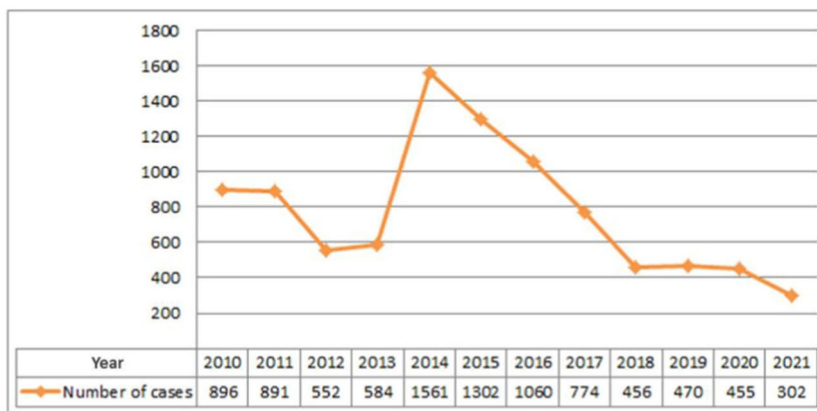


FIGURE 5 Prevalence of Leishmaniasis by area of residence ($p < 0.05$).

Altogether, the number of lesions, type of treatment, and the pattern of cities with the highest number of cases at the time of the pandemic showed no statistically significant difference, in comparison with before the COVID-19 era (see Appendix A).

3.1 | Operational definitions, color codes, and COVID-19 control strategy in region

The National Coronavirus Control Headquarters set out three main criteria for coloring the regions in epidemics: (1) the number of new cases per 100,000 people in the last 14 days, (2) the number of new hospitalization cases per day, and (3) the percentage of positive tests in the last 14 days. In this sense, the first two criteria are more important and expected. Each color demonstrates some critical steps that must be taken to manage the epidemic appropriately. For instance, the red color not only signifies usual public health measures, including masks and social distancing, but also traveling is strictly inhibited, sales are prohibited except for food-based markets, schools and offices must shut down, and family communication is restricted, and people should stay at home (Figure 6).

The color codes of cities' status during the coronavirus pandemic are usually seen in five categories (color) of red, yellow, orange, blue, and white that are assigned based on the rate of virus infection in the region (city) (see Appendix A for more definition).

3.2 | The strategic Leishmaniasis plan and regional data in Ilam

The strategic Leishmaniasis plan in the province is designed in three parts, to provide desirable healthcare services and improve the level of health, to raise the awareness of employees, department and community officials, and to enhance the internal and external coordination. These sections were almost substantially affected during the COVID-19 pandemic.

In this study, the following variables were collected: number of CL cases before and after the pandemic and monthly detection number of cases, number of lesions, lesion location, age, sex, occupation, city, type of population (urban, rural or nomadic centers) year of diagnosis, type, and duration of local or systemic treatment (Figures 1–5, Table 1; also see Appendix A data).

Data quality checks were performed with the participating centers via two experts. Characteristics of CL cases in the province are shown in Figures 7 and 8.

3.3 | The regional Leishmaniasis data in Ilam

Based on field studies, almost all CL cases in the province are *L. major*, and the highest number of cases was observed in January, followed by February and December. The highest incidence of CL in Ilam province occurred in 2014 (269.6 per 100,000 populations), and the number of infected cases gradually decreased to 133.4 per 100,000 populations in 2017 (Figures 9 and 10, Table 2).

Previously in 2014, a peak of CL incidence was encountered in Ilam province, while it declined in the subsequent years through the implementation of adequate control measures. Reportedly, sand fly bites, from sunset to sunrise, peak twice per year, first in April and May and the next in September. The annual activity record of CL in

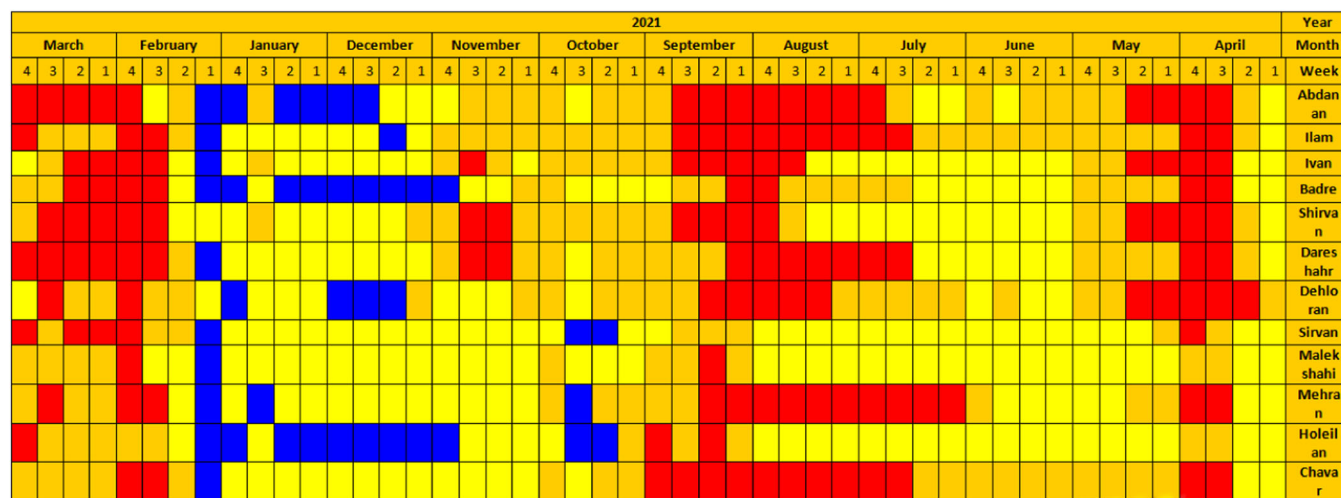


FIGURE 6 Prevalence status and related restrictions introduced to prevent the spread of COVID-19 infection in cities of Ilam province (Red [R]: very risky, Orange [O]: risky, Yellow [Y]: moderate risk, Blue [B]: low risk, White [w]: safe) *(1: April, 2: May, 3: June, 4: July, 5: August, 6: September, 7: October, 8: November, 9: December, 10: January, 11: February, 12: March).

TABLE 1 Comparison of coronavirus and Leishmaniasis monthly data in 2020 and 2021.

	Leishmaniasis		COVID-19	
	2020	2021	2020	2021
April	5	15	300	6929
May	9	20	403	4504
June	6	9	929	1371
July	19	11	3643	2508
August	21	14	2414	8845
September	17	23	2123	7566
October	28	36	4241	4021
November	21	34	6983	2965
December	74	32	2552	928
January	115	59	802	502
February	83	31	968	7994
March	57	18	1379	2575
Total	455	302	26,737	50,708

Ilam showed that *Phlebotomus papatasi* and *Tatera indica* are the main vector and reservoirs in the area, respectively. The pre-patent period of CL is 2–8 months, depending on the type of CL (rural or urban). Noticeably, most CL cases were observed in winter, particularly in January (Figure 11), and in the extremities (hand and leg). The male-to-female ratio was reported to be 1.61/1 (Appendix A data). Mehran and Dehloran possess similar weather conditions for sand fly breeding; hence both are hotspots for CL, so over 50% of patients were found in these regions. Other parts of Ilam province have high altitudes and colder weather. Curiously, Ilam city has a common border with Iraq, a neighboring country, and visitors have to pass

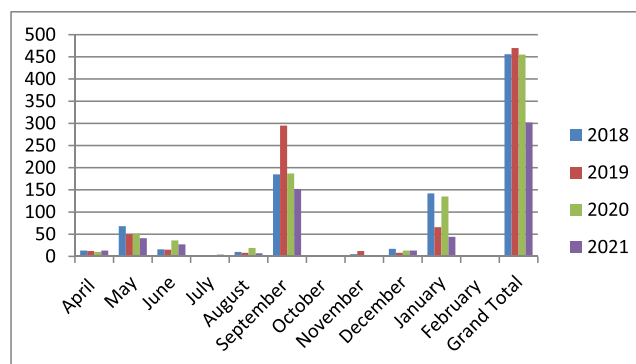


FIGURE 7 Monthly distribution of CL cases in Mehran, Iran, 2014–2018. CL, cutaneous leishmaniasis.

from this city to reach pilgrim destinations in Iraq, increasing the chance of CL transmission.

The sudden increase in cases of Leishmaniasis when the COVID-19 condition is blue (safe) may be due to the delayed referral of patients who have been unable to visit diagnostic and treatment centers during the red and orange days (Figure 12). In almost all cities of the province, the number of CL cases detected in 2019 (at this time, a pandemic has not yet reached Iran and Ilam) decreased, compared with 2018 (year-on-year chart to 1234). While the increase or decrease in cases reported in 2020 (at this time, a pandemic has entered the country and the province, and various restrictions/interventions have been imposed) has no specific pattern compared to 2019. Reports of CL cases may increase (Mehran and Ivan) or decrease (Dehloran) in some cities, while in some areas, there were no significant changes (Ilam and Abadan).

By analyzing the available data, we examine the relationship between the SARS-CoV-2 pandemic and the number of reported cases of CL due to various factors such as time and the number of COVID-19

FIGURE 8 Analysis of characteristics of patients with cutaneous Leishmaniasis in Ilam province (season, year, and month of diagnosis of the disease).

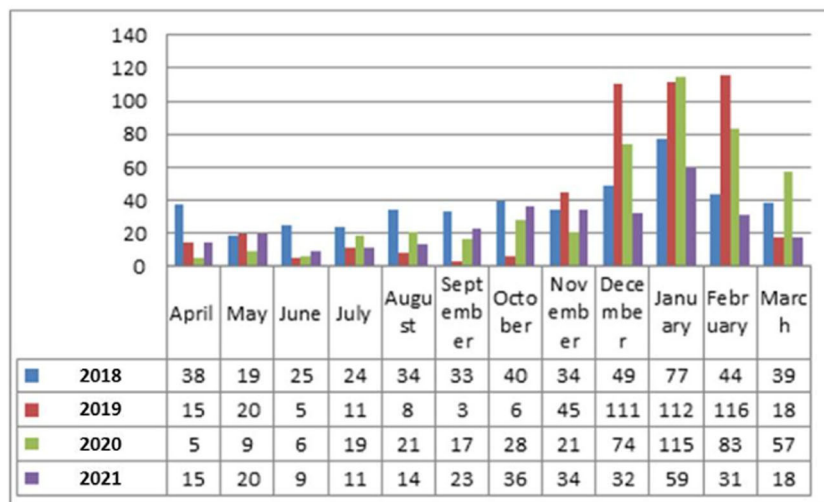


FIGURE 9 Cases of Leishmaniasis per year in different cities of the province.

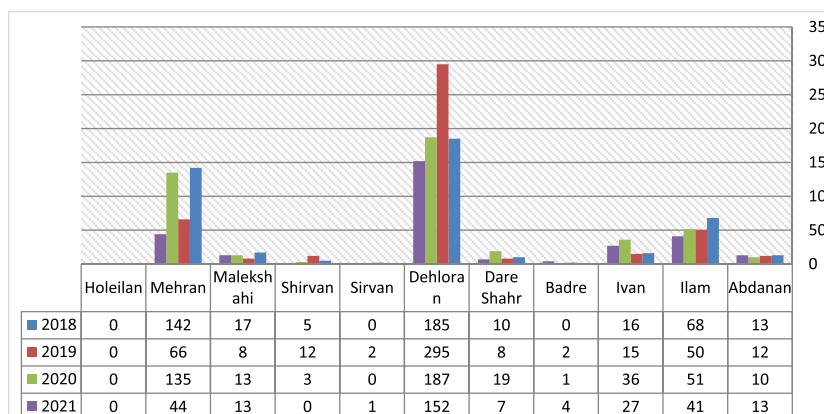
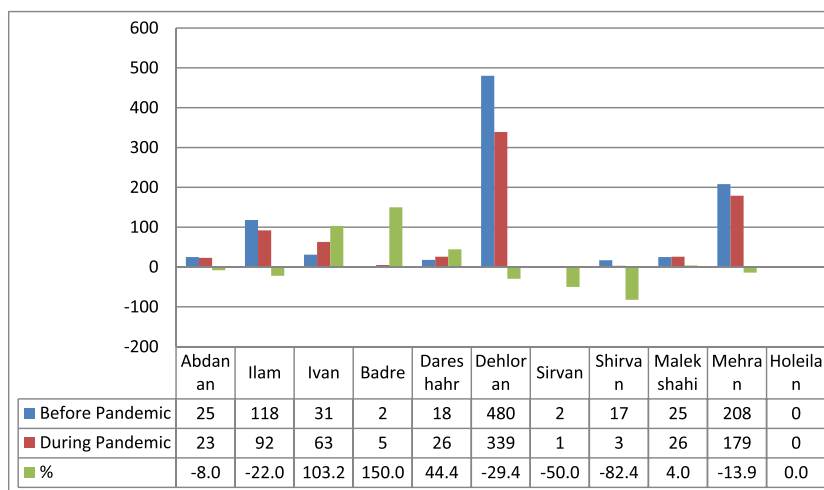


FIGURE 10 Cases of Leishmaniasis in different cities of the province before and during the pandemic.



control programs. These interventions include home quarantine, lockdown, office closure, and/or fear of developing COVID-19 (in case of referral to a hospital/health center to diagnose or treat Leishmaniasis), as well as the negative impacts of a current pandemic on Leishmaniasis control and training programs (such as spraying, implantation, rodent control, and.... due to budgetary reasons or personnel involvement in

pandemic control operations) and the status of active and inactive disease detection programs (Figure 12).

Since the beginning of the pandemic and its arrival in Ilam, active and inactive Leishmaniasis prevention/control programs have been disrupted or even stopped, which can have a decreasing effect on the number of patients reported in 2020 and 2021.

سال City	2018		2019		2020		2021	
	Female	Male	Female	Male	Female	Male	Female	Male
Abdanan	6	7	1	11	2	8	6	7
Ilam	19	49	11	39	22	29	10	31
Ivan	1	15	6	9	13	23	10	17
Badre	0	0	0	2	1	0	0	4
Dareshahr	0	10	4	4	10	9	1	6
Dehloran	69	116	117	178	68	119	61	91
Sirvan	0	0	1	1	0	0	1	0
Shirvan	2	3	3	9	1	2	0	0
Malekshahi	5	12	2	6	5	8	6	7
Mehran	52	90	29	37	65	70	19	25
Holeilan	0	0	0	0	0	0	0	0
Total	154	302	174	296	187	268	114	188

TABLE 2 Chang in number of Leishmaniasis cases by sex in different years.

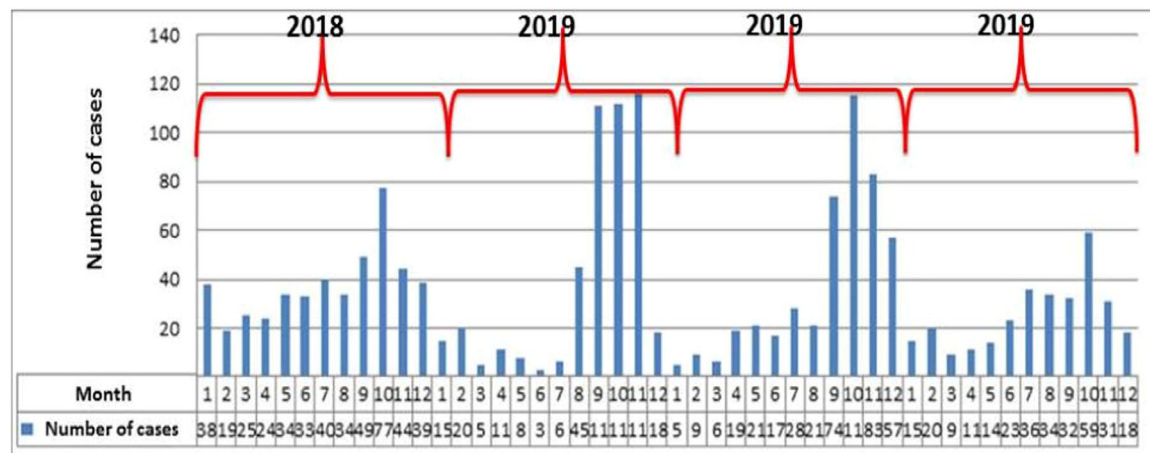


FIGURE 11 Monthly comparison of CL cases trends and peaks before and after the pandemic from 2018 to 2021 (1: April, 2: May, 3: June, 4: July, 5: August, 6: September, 7: October, 8: November, 9: December, 10: January, 11: February, and 12: March). CL, cutaneous leishmaniasis.

Based on our results, most CL cases were diagnosed in winter, especially in January. In contrast, June–August was the peak of CL incidence in Ilam in 2015. This exceptional situation occurred after frequent earthquakes in 2015 in this area and people slept outside of their buildings in the parks, streets, and so on, which imposed sand fly bites. Our data indicated that the burden of CL had been noticeably reduced during 5 years of 2014–2018 in the region as a result of extensive and efficient interventions. Knowledge and attitude of health workers in Ilam about Leishmaniasis was remarkably high. However, the overall knowledge of the public and new healthcare personnel on the CL preventive strategies was affected in endemic areas (Figures 13 and 14, Table 3). Job closures did not include military personnel, and the number of cases in such population did not change so much, because most of them live in border areas, outside of urban homes and in military settlements where it is not possible to properly care for or prevent the entry of insects, as well as

these areas are also endemic for CL. Despite no recorded information, oral interviews with officials and staff of healthcare centers suggested that the number of spraying operations against vector mosquitoes, rodent nest destruction, training workshops, baiting, and rodent control operations during pandemic times have been reduced or even totally suspended.

Infection cases reported in 2021 (at this time, it is almost 2 years since the beginning of the pandemic in the country and the province, different restrictions have been applied with different severity and quality, and several peaks of COVID-19 disease have occurred) decreased compared to 2020, although there was no significant change in some areas.

All together, analyzed information extracted from registered CL data 2 years before the COVID-19 pandemic and two years after its onset showed no fixed pattern in detecting CL cases in Ilam province. This trend has decreased in different proportions in Dehloran,

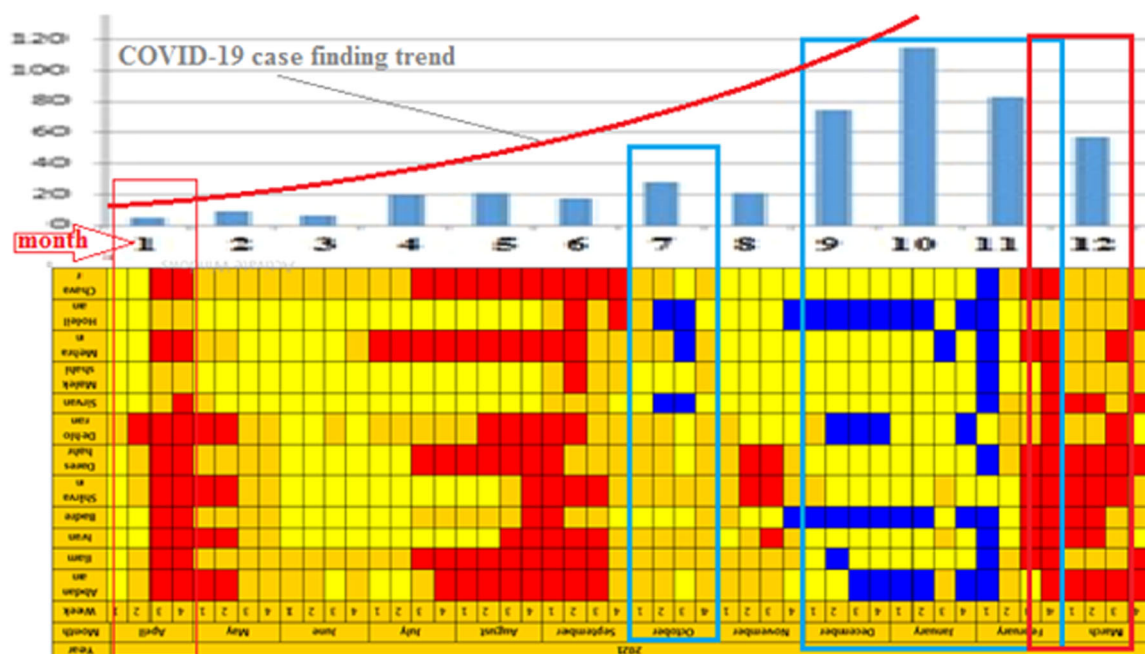
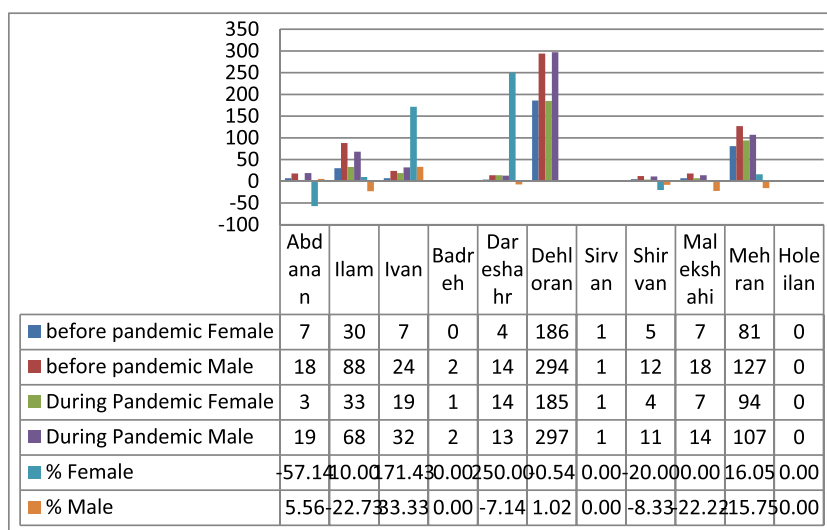


FIGURE 12 COVID-19 restriction strategy status and CL case detection. CL, cutaneous leishmaniasis.

FIGURE 13 Cases of Leishmaniasis in different cities of the province before and during the pandemic based on changes in different sex.



Mehran, Sirvan, Ilam, Abdanan, and so on, and has increased in Ivan, Badreh, and Malekshahi. In this sense, the highest increase belongs to Badreh (+150%) and Ivan (+103%), whereas the highest decrease is related to Shirvan (-80%), Dehloran (-29%), and Ilam (-22%). Nevertheless, in some cities, the determination of CL incidence pattern was not feasible due to the lack of sufficient registered cases or incomplete statistics (Figure 13; $p < 0.05$).

During the first 2 years of the pandemic, in general, and on most occasions, the increase in coronavirus cases was accompanied by a decrease in the number of detected CL cases, as shown in Figure 14. During 2018–2021, the highest number of reported cases of Leishmaniasis occurred in December, January, February, and March; however, in 2021, the reporting rate in these months has decreased

compared to 2020. In total, there observed substantial heterogeneity in the number of reported CL cases during SARS-CoV-2 infection rather than years before the pandemic, which may result from the diversity and differences in parameters affecting the prevalence and reporting of CL in addition to the different burden of COVID-19 infection in each city of Ilam province ($p < 0.05$).

4 | DISCUSSION

Regrettably, those countries endemic regarding NTDs, mainly in Africa, South America, and the Middle East, could not fully adopt efficient control measures to limit the spread of SARS-CoV-2

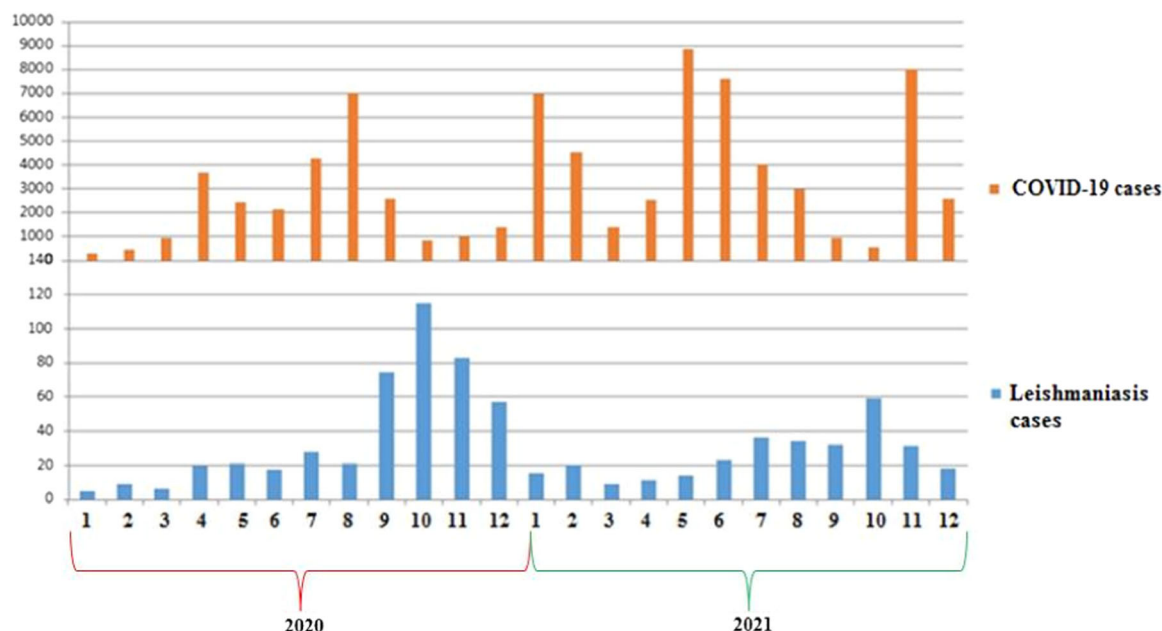


FIGURE 14 Monthly comparison of coronavirus cases trends and peaks against reported cases of Leishmaniasis (1: April, 2: May, 3: June, 4: July, 5: August, 6: September, 7: October, 8: November, 9: December, 10: January, 11: February, and 12: March).

TABLE 3 Total numbers of CL cases before and after the pandemic with percent change.

	Total before pandemic	Total After pandemic	%
Abdanan	25	23	-8.0
Ilam	118	92	-22.0
Ivan	31	63	103.2
Badre	2	5	150.0
Dareshahr	18	26	44.4
Dehloran	480	339	-29.4
Sirvan	2	1	-50.0
Shirvan	17	3	-82.4
Malekshahi	25	26	4.0
Mehran	208	179	-13.9
Holeilan	0	0	0.0
Total	926	757	-18.3

Abbreviation: CL, cutaneous leishmaniasis.

infection.³⁴ The action plan for Leishmaniasis was prepared in 2014 to reduce the CL cases by 90% of the current situation over the next 5 years (until the end of 2019). However, such a prospect was not achieved in the targeted years. In the case of reduced health services, the mortality due to viral infection and other preventable communicable diseases increases substantially.^{26,35,48,53,54,70} The extent of elevated disease incidence depends on the infection's endemicity and local transmission conditions.¹⁴

From November 21, 2020, the Coronavirus Control Headquarters implemented extensive national closure and restrictions as part of the Comprehensive Corona Virus Intelligence Management Plan. On March 22, 2020, the Ministry of Health and Medical Education announced that level three quarantine (red) was set to implement against Coronavirus. The gender-based number of CL cases was remarkably different among cities, regardless of the general pattern of changes in the number of cases reported between 2 years before and 2 years after the beginning of the pandemic in Ilam province; for instance, the number of women CL cases decreased in Abdanan (-57.14%), while men CL cases increased (+5.56%). Also, in Darrehshahr and Ilam cities, women cases increased (+250% vs. +10%), while men showed decreasing rates (-7.14% vs. -22.73%). In Ivan, CL cases increased in both gender, +171.43% (men) and +33.33% (women). However, in Shirvan, men (-8.33%) and women (20%) showed a declining trend. (Charts: percentage increase or decrease in cases of Leishmaniasis by sex in the previous 2 years and 2 years during the corona; $p < 0.05$).

Based on the literature, most isolated bacteria possessed high antibiotic resistance to common antibiotics and various studies on the prospective antibiotic consumption during the first wave of the COVID-19 pandemic described changing trends over time.^{71,72} Several investigations have been performed to assess the likely impact of the SARS-CoV-2 pandemic on different facets of life, health, and underlying health system parameters such as costs, antibiotic resistance, physiological effects, and possible interaction with other diseases.^{16-18,29,30,35,48,49,53,54} There is still no specific, completely safe, and appropriate drug, method, or vaccine for the treatment or prevention of CL, as well as the occurrence of secondary infections at the wound site and the need to take other

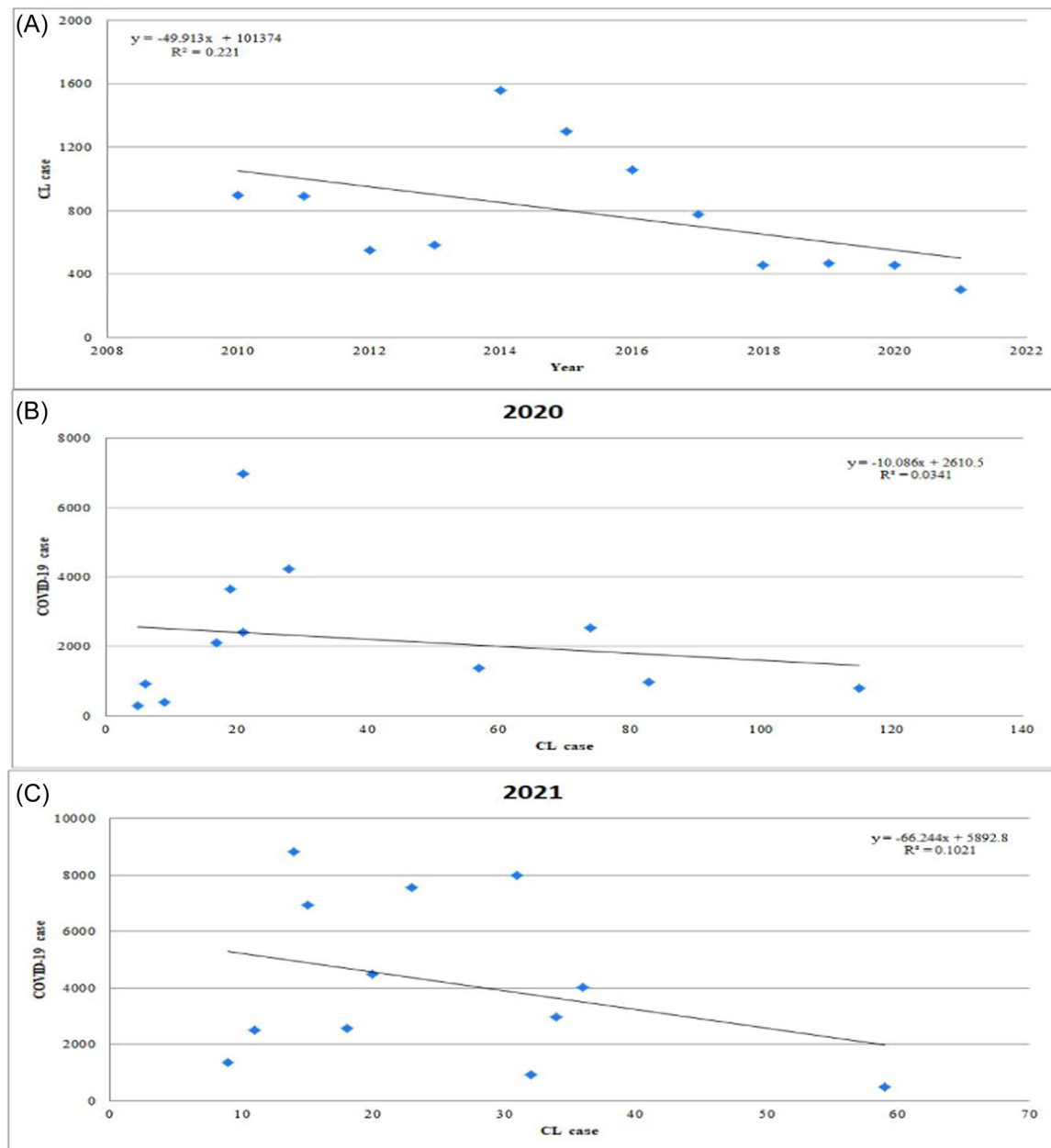


FIGURE 15 Association between CL cases with year (A) and COVID-19 cases in 2020 (B) and 2021 (C). CL, cutaneous leishmaniasis.

antibiotics, along with the emergence of resistance to anti-leishmanial and antibacterial agents, makes the treatment of this infection more complicated.^{73–79} Despite the introduction of several types of different treatments (Traditional medicines, treatment with stem cells and their derivatives, chemical compounds, cryotherapy, etc.), it still seems that prevention of contracting the infection is still a more cost-effective way to deal with this disease.^{72,74,80–84} In Ilam province, Mehran and Dehloran are tropical areas and one of the most significant spots regarding CL due to the movement of pilgrims towards and outwards of the Iran-Iraq border until sunset and late at night, which coincides with the activity of CL biological vectors. Therefore, natives and travelers will be exposed to sand fly bites and Leishmaniasis.

Due to the current pandemic, NTD-associated funding has been reduced or shifted towards prevention strategies against COVID-19 due to the enormous financial challenges faced by the world.⁸⁵ Dissimilar to infections such as tuberculosis, home quarantine, and work lockdown did not play a significant role in the elevated household transmission of CL or did not cause misdiagnosis due to the resemblance of symptoms. The major challenge is shifting the health resources and personnel to combat COVID-19 and cure SARS-CoV-2 cases, which may substantially disrupt anti-Leishmaniasis activities such as destroying rodents nests and baiting or/and fighting and control of insect vectors (interior residual sprays and insecticide-treated nets). In specific events, such as the earthquake in 2004 or the development of new agricultural projects, leading to the

establishment of suitable propagation sites for mosquito vectors, a newly emerging focus of CL for possible human transmission was created in Abdanan County in Ilam province.⁸⁶ These problems raise the concern that the COVID-19 pandemic and its complications could act as the expanding cause of new foci of CL and other NTDs in the affected regions.

In 2022, 57% of CL endemic countries (51 out of 89 countries) reported their CL data to WHO until 20 October. The highest reporting rates in endemic countries were seen respectively in the Eastern Mediterranean Region (EMR), AMR, African Region (AFR) and in, South-East Asia Region and the European Region (EUR) (89%; 16/18, 86%; 18/21, 53%; 10/19, 40%; 2/5 and 68%; 17/25, respectively). Also, Western Pacific Region (WPR) has no data reported. 221,614 autochthonous and 339 imported new CL cases (sum: 221,953) were reported to WHO in 2021.^{87–89} More than 95% of the new CL cases were reported from EMR and AMR. Pakistan, Afghanistan, Iraq, Brazil, Colombia, Algeria, Peru, and Syria each reported >5000 CL cases. Usually, there was a routine, increasing trend in the number of new CL cases reported at the annual global level, but it continued with a sharp decrease in the number of cases during the COVID-19 pandemic.⁸⁷ During the COVID-19 period in 2021, about a 44.5% decrease in CL cases was reported in AMR regions. There was a sharp decrease in the number of CL cases in AFR in 2021.⁹⁰

In a similar study in Brazil, there was an increase in the number of clinic visits due to Leishmaniasis in five regions, from the 2020 pandemic period (over 57%) compared with 2017–2019 years. Curiously, this increasing trend was related to the tegumentary Leishmaniasis, while consultations associated with visceral Leishmaniasis decreased considerably. This shows that the epidemiological surveillance of NTDs cannot slow down in the country.³⁶ Annually, a large number of Iranian Shia pilgrims travel to Iraq from this area to participate in one of their most important religious ceremonies. This trip has coincided with the seasonal activity of sand flies in recent years. So, CL could be a serious threat to pilgrims on these occasions.⁹¹ Since the COVID-19 pandemic has forced healthcare services and finances toward prevention strategies, including vaccination campaigns against this devastating viral infection, there are progressive concerns regarding the considerable disruptions in the control programs against various parasitic diseases, such as CL, and the subsequent rise in affected patients.^{55,58}

As Figure 15 showed, based on simple linear regression model, there is a negative trend association between CL and year (b : -49.91; R^2 : 0.221). Also, there is a negative association between CL and COVID-19 cases during 2020 (b : -10.09; R^2 : 0.034) and 2021 (b : -66.24; R^2 : 0.102).

5 | CONCLUSION

Since January 2019, the SARS-CoV-2 viral pandemic has caused substantial disruptions to the healthcare systems in several aspects, including control of NTDs, across the globe. Nevertheless, due to the

limited data, we cannot confirm or deduce a decreased trend in treatment after the COVID-19 pandemic. Throughout a year of CL transmission, the environmental interventions directed towards mosquito control, exterminating stray dogs, and eliminating rodent nests must be done correctly. Our cross-sectional registry-based study pointed out potential gaps and highlighted urgent demands to adapt health services to ensure the implementation of essential control strategies against CL. Other factors, such as the repurposing of diagnostic and clinical services, the health personnel focus on COVID-19, and changes in patients' health-seeking behavior, may play a role and demand further attention. The effect of increasing or decreasing coronavirus cases on the reporting rate or being infected with Leishmaniasis does not emerge immediately. Compared with the onset of the epidemic, the registration and case reporting rate was most affected, possibly due to the reduced hospital visits for several reasons (lockdown programs, public fear of COVID-19, or reduced access to health and diagnostic services). Moreover, in the long-term, the health care system, including anti-Leishmaniasis control programs (interventions and activities such as rodent nest destruction, baiting, controlling and fighting vector insects), is disrupted due to system fatigue, budget shifts and focus of resources on controlling the coronavirus epidemic; thereby, the likelihood of infections such as CL may increase. Finally, there was more heterogeneity in the number of reported CL cases during the COVID-19 pandemic than before, which may arise from the diversity and differences in parameters affecting the prevalence and reporting of CL and the different burden of COVID-19 epidemic in each city of Ilam state.

Previous reports demonstrated the effectiveness of the rodent control program implementation, the retraining courses, and the implementation of health education programs for healthcare personnel and inhabitants of endemic regions in controlling CL.^{62–66} Hence, establishing and empowering these actions could be recommended to control CL in Ilam County and other endemic regions.

5.1 | Limitation of study

A limitation or bias in the data, like our study, is that preventive strategies are modeled only based on their potential correlation with the transmission of infection; and analysis of cost, cost-effectiveness, the availability of the additional medicines, diagnostics, and interventions that might be needed to implement is not explored. Therefore it is possible that some interventions or parameters modeled in our study might not be widely implementable.

AUTHOR CONTRIBUTIONS

Morteza Shams: Conceptualization; data curation; formal analysis. **ayoub rashidi:** conceptualization; data curation; formal analysis. **Jasem Mohamadi:** Conceptualization; data curation; formal analysis. **Mohamad Moradi:** Data curation; formal analysis. **Reza Pakzad:** Data curation; formal analysis. **Razi Naserifar:** Conceptualization; data curation; formal analysis. **Jahangir Abdi:** Conceptualization; data curation; formal analysis. **Fariba Ghelichi:** Conceptualization; data curation; formal analysis. **Arezo**

Bozorgomid: Conceptualization; data curation; formal analysis. **Nahid Maspi:** Conceptualization; data curation; formal analysis. **Azra Kenarkoohi:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; writing—original draft; writing—review and editing. **Yasin Mohammadi:** Conceptualization; data curation; formal analysis; methodology. **Amir Abdoli:** Conceptualization; data curation; formal analysis; methodology; supervision; writing—original draft; Writing—review and editing. **Shahab Falahi:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; writing—original draft; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

TRANSPARENCY STATEMENT

The lead author Shahab Falahi affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

ORCID

Razi Naserifar  <http://orcid.org/0000-0001-6946-9083>

Azra Kenarkoohi  <http://orcid.org/0000-0003-4077-9824>

Amir Abdoli  <http://orcid.org/0000-0003-4326-4586>

Shahab Falahi  <http://orcid.org/0000-0002-3764-2168>

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APPENDIX A

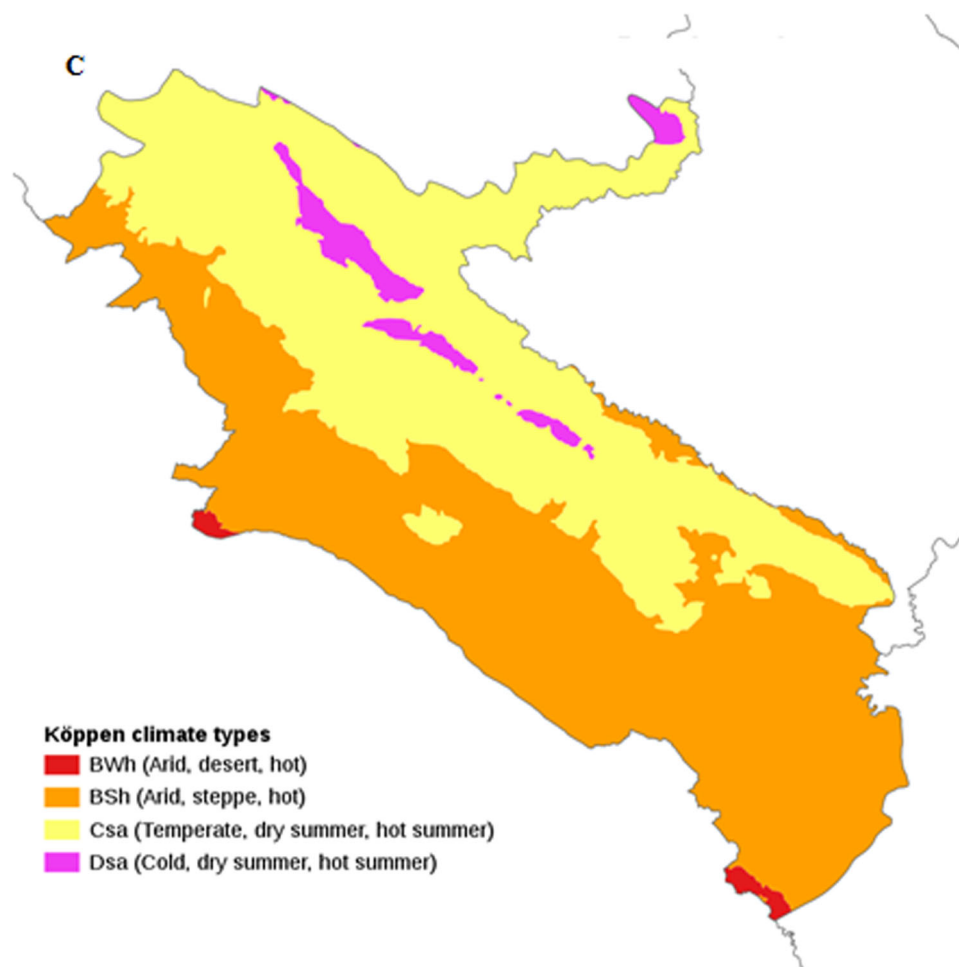
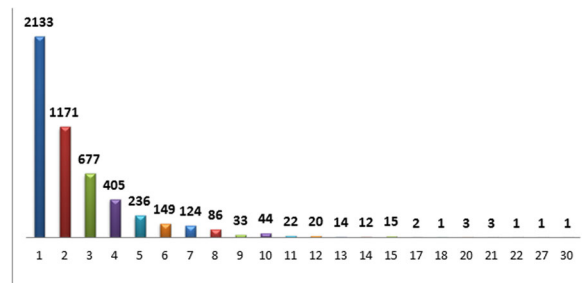
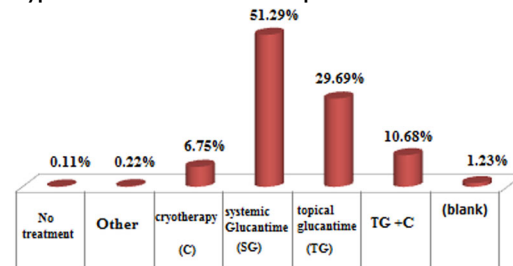


FIGURE A1 Köppen climate types of the Ilam province in Iran.

Prevalence of leishmaniasis based on number of lesions



Types of treatments used for patients with leishmaniasis



Percentage of changes in total leishmaniasis cases 2 years before and 2 years during the pandemic

%	During Pandemic		Before Pandemic	
-8.0	23		25	Abdanan
-22.0	92		118	Ilam
103.2	63		31	Ivan
150.0	5		2	Badre
44.4	26		18	Dareshahr
-29.4	339		480	Dehloran
-50.0	1		2	Sirvan
-82.4	3		17	Shirvan
4.0	26		25	Malekshahi
-13.9	179		208	Mehran
0.0	0		0	Holeilan
-18.3	757		926	Total

Increase or decrease in cases of leishmaniasis by sex in the previous 2 years and 2 years during the coronavirus pandemic

% Male Female		During Pandemic Male Female		Before Pandemic Male Female		
5.56	-57.14	19	3	18	7	Abdanan
-22.73	10.00	68	33	88	30	Ilam
33.33	171.43	32	19	24	7	Ivan
0.00	0.00	2	1	2	0	Badre
-7.14	250.00	13	14	14	4	Dareshahr
1.02	-0.54	297	185	294	186	Dehloran
0.00	0.00	1	1	1	1	Sirvan
-8.33	-20.00	11	4	12	5	Shirvan
-22.22	0.00	14	7	18	7	Malekshahi
-15.75	16.05	107	94	127	81	Mehran
0.00	0.00	0	0	0	0	Holeilan
-5.69	10.06	564	361	598	328	Total

Monthly distribution of CL cases in Mehran, Iran, 2014–2018

2021	2020	2019	2018	
13	10	12	13	April
41	51	50	68	May
27	36	15	16	June
4	1	2	0	July
7	19	8	10	August
152	187	295	185	September
1	0	2	0	October

(Continues)

2021	2020	2019	2018	
0	3	12	5	November
13	13	8	17	December
44	135	66	142	January
0	0	0	0	February
302	455	470	456	Grand total

The status of leishmaniasis cases 2 years before the coronavirus pandemic and during the pandemic by month

2021	2020	2019	2018	Month
15	5	15	38	April
20	9	20	19	May
9	6	5	25	June
11	19	11	24	July
14	21	8	34	August
23	17	3	33	September
36	28	6	40	October
34	21	45	34	November
32	74	111	49	December
59	115	112	77	January
31	83	116	44	February
18	57	18	39	March
302	455	470	456	Grand total

Some measures taken regarding leishmaniasis programs in the province

- Focus on insect control activities, fauna and frequency research and... in the border areas of the province (Mehran and Dehloran)
- Accelerate the process of equipping the entomology laboratory in connection with the study of catches and determination of fauna (species) and frequency with the help and support of the Center for Disease Management
- Cooperation and coordination with educational, research, etc., to document studies and create a database of entomological studies
- Establishment of a leishmaniasis research center as one of the leishmaniasis centers with the cooperation and advice of the Center for Disease Management

Establishment of Zoonotic Disease Research Center at the University of Medical Sciences

- Holding internal and external committees for seekers
- Registration of cases in the portable system of the Disease Management Center

(Continues)

- Training of public and nongovernmental sector physicians, experts and associates of affiliated cities, health care providers, staff of Leishmania diagnostic laboratory with the presence of professors of the Disease Management Center of the Ministry of Health

- Preparation and distribution of educational pamphlets. Install banner and...

- Leishmania test in the laboratories of the province

- Spraying high-risk areas of leishmaniasis on the outskirts of Dehloran and Mehran based on the protocol

- Implementation of implantation and rodent control plan with the assistance and presence of professors of the Ministry of Health in the target cities

- Distribution of insect repellent spray among military personnel stationed in endemic areas

Operational definitions, color codes, and COVID-19 control strategy in region

The color codes of cities status during the coronavirus pandemic, usually seen in five categories (color) red, yellow, orange, blue, and white that are usually assigned based on the rate of virus infection in the region (city). The color coding criterion of the cities is based on the ratio of hospitalized patients to the total population number in the region; also changing the color of cities is naturally not a complete and accurate criterion because it does not indicate the real amount of danger and the full burden of the epidemic in the regions. According to the approvals of the National Coronavirus Control Headquarters, the blue status has been added to the previous color schemes, and accordingly, the cities will go from yellow (medium risk) to blue (low risk) status, and then turn white if the appropriate conditions continue. In this classification, after passing the yellow status, cities do not turn directly to the white code; but, they will first go into the blue status. The number of patients in blue is less than in yellow cities, but does not mean that the virus is gone in that area.

Green: This is an area where no new COVID-19 cases have been reported in the last 28 days, or have less than one positive case per 100,000 people.

White: According to the recommendations of the Ministry of Health, the city is in a white (low risk) situation that has both of the following two conditions in the last 2 weeks:

Condition 1: The average acceptable daily hospitalization rate is a maximum of 1 case per 100,000 population. For example, in a city with a population of 200,000, an average of 2 new patients should be admitted daily.

Condition 2: The average number of daily hospitalizations should be a maximum of 1 case per 100,000 population, which means that a city of 200,000 people should have a maximum of 14 hospitalizations during the past 2 weeks (including suspicious and definite cases). White status does not mean that the region is safe.

Yellow: In areas with yellow conditions, one or more new cases of the disease with positive PCR test are seen, and the risk is as expected. The acceptable number of definite new cases per 100,000 people is 1–9 cases.

Orange: The acceptable number of new definitive cases of the disease is 10 to 24 per 100,000 people and the overall epidemic trend is rising.

Red: The acceptable number of new cases of the disease is more than 25 per day per 100,000 population and the epidemic trend is progressive.

Nonnative cars are currently banned in the red and orange cities, but there is no ban on going to the yellow and blue cities. Yellow code means moderate risk status and in this situation, only level 4 jobs will be closed. Orange status means high-risk situation and levels 3 and 4 jobs will be closed; as well as red notice means very high-risk status in which all jobs (except essential level 1 jobs) will be closed. Also, the entry and exit of nonnative and native cars to/from the orange and red cities will be prohibited. These codes and colors must be used correctly and the necessary actions must be taken for each situation.