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The Economic Burden of Cutaneous Leishmaniosis: Report from a Developing Country

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Abstract

Background: Considering the high prevalence of cutaneous leishmaniasis in tropical and subtropical countries and the urgent need for an economic approach to the treatment sector, this study aimed to investigate the economic burden caused by this disease in Northeast Iran.

Methods: This cross-sectional study was conducted on 3558 patients with cutaneous leishmaniasis whose data were registered in the disease surveillance system at Mashhad University of Medical Sciences, Mashhad, Iran. The disease care model was designed from the stage of suspected disease to diagnosis, treatment, treatment/care of disease complications, treatment/care of drug side effects, disease recurrence, and drug resistance. Then, the direct costs were calculated.

Results: Overall, 7.5 billion Rials (equal to $750,000) have been spent on providing health care services to 3558 patients with leishmaniasis. The per capita cost of diagnosis/treatment of the disease was 1,600,100 Rials (equal to $160), the per capita cost of care/management was 505,902 Rials (equal to $50), and the per capita cost of cutaneous leishmaniasis disease was calculated as 2,106,002 Rials (equals to $210).

Conclusion: Leishmaniosis has a considerable economic burden on society and the healthcare system. Considering that the predisposing factors are avoidable, it is possible to reduce the economic burden by using less expensive and effective solutions.

Keywords: Leishmaniosis, Economic Burden, Iran

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Introduction

In the second epidemiologic transition of diseases, humans encountered a significant decrease in the occurrence of communicable diseases and an increase in the spread of non-communicable diseases (1-10). However, the increased incidence and epidemic occurrence of infectious diseases in the third epidemiologic transition (11-14) was a confirmation of the fact that the transients of diseases are not linear but a cyclical process. A significant portion of these emerging diseases are zoonosis diseases, which heavily strain health systems. The health, social, and economic consequences of epidemics in the first 2 decades of the present century, such as Middle East respiratory syndrome, Crimean-Congo hemorrhagic fever, influenza, and other emerging and reemerging zoonosis diseases emphasize the importance of these diseases.

Leishmaniasis is one of the most common, hence, neglected diseases in tropical regions (15). Humans are infected through the bite of the female ground mosquito, which usually lives in wooded areas, caves, and shelters such as wall cracks and nests of small rodents. The disease can be seen in 4 forms—cutaneous (CL), diffuse cutaneous,

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↑What is "already known" in this topic:
Leishmaniasis is one of the most common, hence, neglected diseases in tropical regions—including Iran. Most studies are focused on the visceral form of this disease.

→What this article adds:
Implementing less costly yet highly effective remedies, such as preventing mosquito bites and integrating health care, could lessen the high economic burden of cutaneous leishmaniasis.

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mucosal cutaneous, and visceral (VL) (16).

One million new cases of this disease occur annually worldwide (16). It was estimated that 350 million individuals were at risk of this disease in 2010 (17), but more recent data suggest that 1 billion people are at risk in endemic areas (18). The disease burden caused by leishmaniosis was estimated to be 2.34 million years in 2010 (15), which was the third rank among neglected tropical diseases and the second cause of death caused by parasites (19). This disease is endemic in 88 countries of the world, but in many of them, not much attention is paid to it, and since it is not fatal, the disease has been forgotten (20). More than a decade ago, 90% of cutaneous leishmaniosis occurred in 7 countries of the world, including Iran (21). In 2021, the situation was not changed much: 9 countries—including Iran—reported >5000 CL cases, which account for 88% of global reported CL cases (22). Among the countries of the Middle East and North Africa region, Iran has the highest prevalence with 18175 cases of CL (Leishmania major), and the second rank after Syria with 8549 CL cases (Leishmania tropical) (23).

In cutaneous leishmaniosis, there are skin ulcers with raised edges that may take several months to heal. Even with successful treatment, a considerable scar will remain (24). People believe that the disease is transmitted through physical contact, thus, sick people are deprived of communication with others. These scars can even influence women's marriage, childbearing, and breastfeeding (25). Considering the emotional and psychological problems caused by scars, physical disability following this disease is considered moderate (20).

This disease imposes a heavy economic burden on families, communities, health systems, and countries—especially developing countries (17). Glucantime is used for treatment, which is an expensive drug and requires multiple injections. Resistance to this treatment is also common (26) and various side effects are reported (15).

Most conducted studies on the economic burden of leishmaniosis are related to visceral leishmaniosis (kala-azar) and few studies have been conducted on the economic burden of its cutaneous form. The cost of treatment per patient is reported to be $15 to $200 in Afghanistan in 2002 (27), $280 in Guatemala in 2001, and $300 in Peru in 2005 (28). In Iran, 2 studies have estimated the financial burden of Leishmaniosis, which is based on a restricted sample size (29).

Considering the high prevalence of the disease in Iran, especially since Khorasan Razavi Province is one of the main centers of this disease in the country due to ecological changes, indiscriminate constructions, urban development, migrations, et cetera, this study was conducted to provide an estimation for the economic burden and costs of leishmaniosis to determine the value of investing in the prevention strategies for public health policymakers.

Methods

This cross-sectional study was conducted using the census method on the data of 3558 patients with confirmed cutaneous leishmaniosis who visited health centers, hospital clinics, outpatient clinics, and hospitals in Khorasan Razavi province from April 1, 2012, to March 31, 2013 (the year 1390 in the Persian calendar). The inclusion criteria were all patients (ie, census method) who have been diagnosed with leishmaniosis in Khorasan Razavi province and were registered in the surveillance system of the vice chancellor for health at Mashhad University of Medical Sciences, Mashhad, Iran. In addition, patients whose information was incomplete according to the study objectives were excluded. The protocol of this study is registered and approved by the Vice Chancellor for Research at Mashhad University of Medical Sciences (ID: 910326) and the ethical committee of Mashhad University of Medical Sciences. All the extracted information from the surveillance system was blinded and the patient names were removed. The national code was used as the unique identifier.

Required variables such as patient's age, sex, nationality, city of residence, type and the number of lesions, time of infection, treatment failure, recurrence after systemic and local treatment, clinical resistance, and discontinuation of treatment were extracted from the health care system of Mashhad University of Medical Sciences. There were 3 executive stages for this study:

1. Determining Incidence Rates

All available data of the cutaneous leishmaniosis in the surveillance system regarding sex, age, city, and other variables were extracted from the checklists and were entered into the SPSS Version 11.5 software, and the rate of occurrence according to the aforementioned variables were calculated. The population covered by Mashhad University of Medical Sciences in the study year (2012/2013) was 4,929,471 individuals and the incidence rates were calculated according to the number of patients.

2. Designing the Disease Care Model from the Stage of the Suspected Disease to Diagnosis, Treatment, Care and Treatment of Disease Complications, Care and Treatment of Drug Complications

At first, by referring to scientific sources—including reference books, scientific articles, and reliable scientific websites—all diagnostic methods, paraclinical diagnostic methods, and treatment methods of old-world leishmaniosis, disease complications, and complications of treatment methods were extracted and the list was compiled separately as follows:

- ***Diagnostic Methods:*** Clinical diagnosis, paraclinical diagnosis, superficial smear, biopsy, leishmania test, cultivation in Novy–MacNeal–Nicolle (NNN) medium, polymerase chain reaction (PCR).
- ***Treatment Methods:*** (A) Systemic treatment—including injectable antimuon meglumine, itraconazole, fluconazole, dapsone, zinc sulfate, amphotericin B, pentoxifylline, azithromycin, omeprazole, allopurinol, and oral miltefosine. (B) Local treatment—including topical glucantime, topical amphotericin, topical paromomycin, topical imiquimod, and hypertonic sodium chloride solution inside the lesion. (C) Physical therapy—including cryotherapy, infrared, carbon dioxide laser, direct electrical stimulation, and ultrasound. (D) side effects of the disease—including disease recurrence, resistance to treatment, and wound

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complications. (E) Complications of the treatment, which include the treatment protocols.

After preparing the list of diagnostic methods, treatment, complications of treatment, and complications of the disease, an expert panel regarding the care of the patients including 5 dermatologists from 2 main academic hospitals affiliated with Mashhad University of Medical Sciences and 2 general doctors who work in health care centers and were responsible for the diagnosis and treatment of leishmaniosis cases was established. Checklists prepared in the fields of diagnostic methods, treatment methods, disease complications, and complications of treatment methods were made available to these experts to specify the diagnostic and treatment methods they use by mentioning the relative frequency of each item. Also, they were asked to state the complications of the disease (complications of the wound) and the complications of the possible treatment methods that they have observed up to that time, as well as the care measures in that field (care interventions). Finally, by summarizing the opinions of the expert panel in the field of diagnosis and treatment of cutaneous leishmaniasis in the province, the final percentage (relative frequency) was calculated based on the average frequency declared in 4 disease care domains.

In addition to the opinions of the panel's experts, the available scientific papers (reference books and scientific journals) were studied to determine the relative frequency of cases where complications from the disease and therapy intervention may arise.

The disease care model was then developed with the assistance of another expert panel that included dermatologists, community medicine specialists, laboratory science specialists, and experts in the health field. This panel included the following: the stage at which the suspected case seeks assistance and refers to the health care system; the initial examination by a doctor; laboratory sampling; paraclinical diagnostic steps; referral to the doctor; the beginning of the treatment phase, which includes systemic and local treatments; paraclinical diagnostic measures to prevent drug side effects; care and treatment of potential side effects; diagnosis and treatment of disease side effects; and periodic and final examinations by doctors.

3. Calculating the Cost of the Disease

At this stage, with the help of the third expert panel consisting of paraclinical specialists, health care experts, experts in vice chancellor for treatment at Mashhad University of Medical Sciences, and pharmaceutical field experts, the costs of each of the detailed measures drawn in the flowchart of the disease model were determined based on obtaining information from service providers (ie, real expenditures were considered not estimations). Then, the total cost was calculated based on the determined costs and the probabilities mentioned in the disease cost flowchart. In addition, to calculate the hospitalization cost, the costs resulting from the hospitalization of all patients with cutaneous leishmaniosis in 2 main academic hospitals of Mashhad University of Medical Sciences in 2013, were extracted by referring to their hospitalization records. Finally, considering the number of leishmaniosis cases, the per capita cost of the disease was also calculated. Due to uniformity, the cost is reported based on rial and dollars. Based on the dollar-rial exchange rate at the time of performing this study (2012-2013), $1 was equivalent to 10,000 Rials.

The complete process of estimating different dimensions of diagnosis and treatment is shown in Figures 1 A and B.

Results

Overall, 3558 patients were included and 7.5 billion Rials (equal to $750,000) have been spent on providing health care services for them.

Based on the analysis, the total cost of diagnosis was 354,505,700 Rials (equal to $35,450). This was 2,972,360,263 Rials (equal to $297,236) for the treatment of leishmaniosis (Tables 1 and 2). In addition, there were 750,924,800 Rials (equal to $75,092) for complications, 2,385,144,300 Rials (equal to $238,514) for other clinical practices, and 8,281,315,123 Rials (equal to 828,131 Rials) for other clinical measures (Tables 3-5).

In another view, the per capita cost of diagnosis/treatment of the disease was 1,600,100 Rials (equal to $160), the per capita cost of care/management was 505,902 Rials

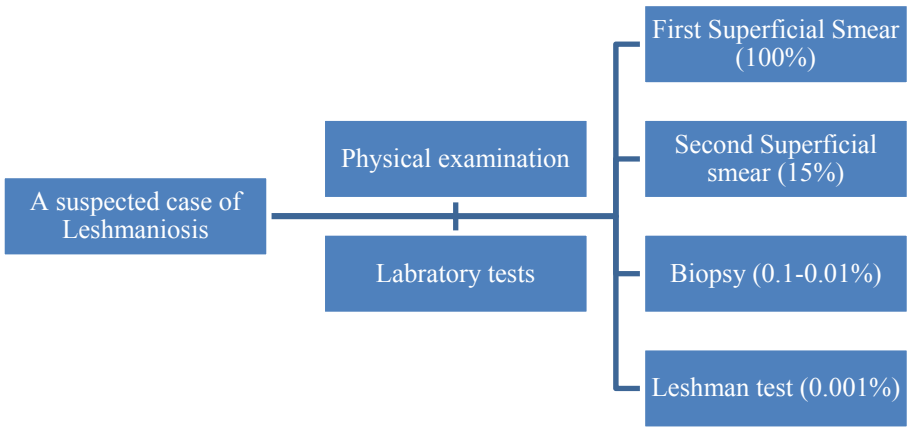

Figure 1A. The flowchart of diagnosing Leishmaniosis with frequency estimation

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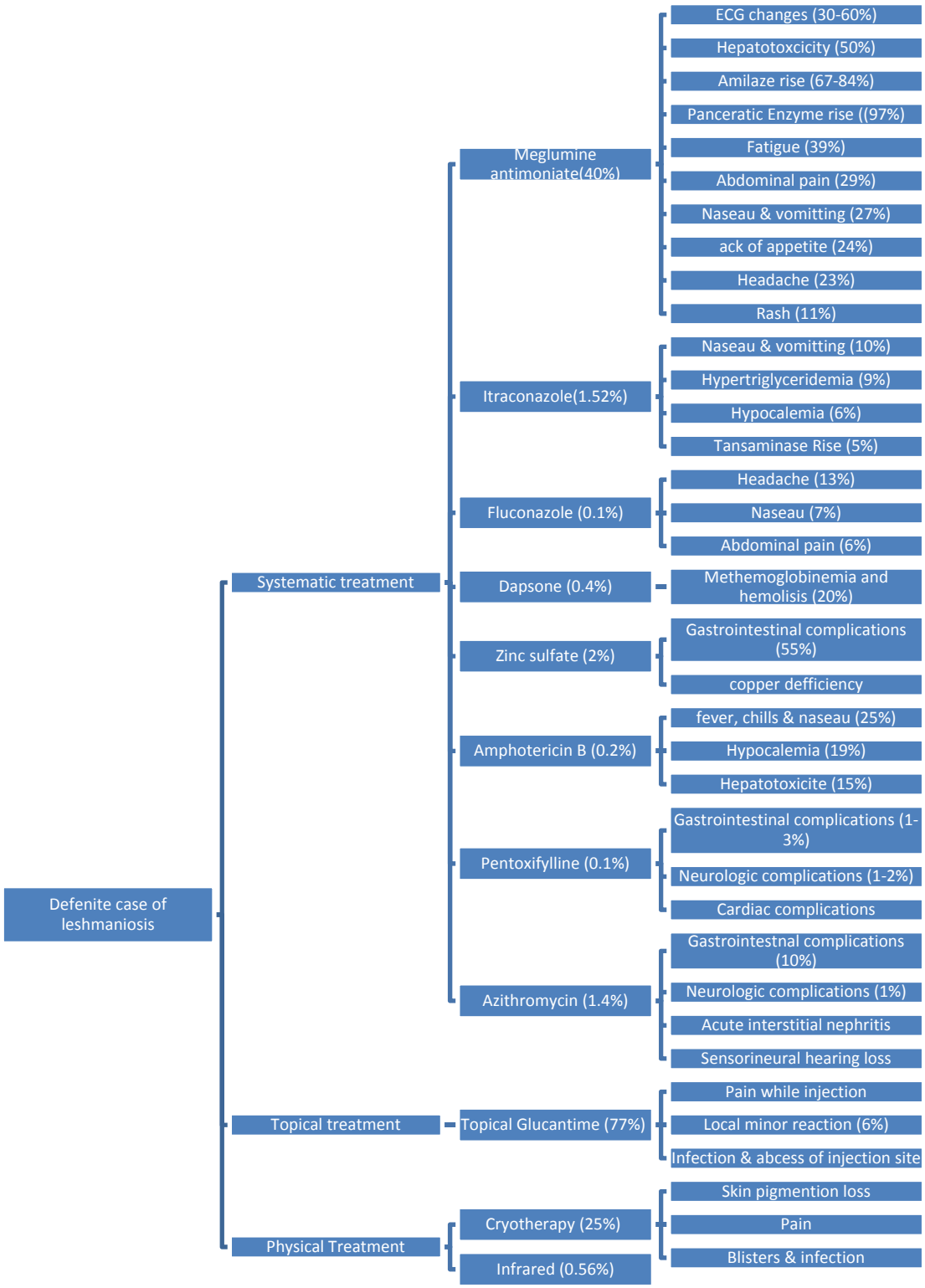

Figure 1 B. The Flowchart of various approaches for the treatment of Leishmaniosis with frequency estimation

(equal to $50), and the per capita cost of cutaneous leishmaniasis disease was calculated as 2,106,002 Rials (equals to $210).

DISCUSSION

According to the results of this study, 3558 patients with cutaneous leishmaniosis were included in the surveillance system in 2013. Considering the population covered by Mashhad University of Medical Sciences in that year, the

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Table 1. The estimation of Diagnosis Cost of Leishmaniosis

Diagnostic Procedure		N (%)	Appointment	Unit Cost (Rials)	Total Cost (Rials)
Clinical	General practitioner	2	2491 (70)	37,000	184,334,000
	Specialist	2	1067 (30)	55,000	117,370,000
Para clinic	Surface smear	first	3558 (100)	13,100	45,299,800
		second	534 (15)	13,100	6,995,400
	Biopsy	1	2 (0.05)	246,700	493,400
	Leishman test	1	1	13,100	13,100
Total					354,505,700

Table 2. The Estimation of the Treatment Cost of Leishmaniosis

Treatment Method		N (%)	Appointment	Unit Most(Rials)	Total Most (Rials)
Systemic	Glucantime	1424 (40%)	3	18,500	1,580,640,000
	Itraconazole	55 (1.52)	35*2	22,145	85,258,250
	Fluconazole	4 (0.1)	30	46,000	184,000
	Dapson	15 (0.42)	60	248,000	3,720,000
	Zinc sulfate	72 (2)	45*3	30,250	2,178,000
	Pentoxifylline	4 (0.1)	30*3	215,200	860,800
	Azithromycin	50 (1.4)	4*15*2	370,000	18,500,000
Topical	Glucantime	2740 (77)	12	303,120	830,548,800
Physical	Cryotherapy	890 (25)	10	416,250	370,462,500
	Infrared	20 (0.56)	10	220,000	4,400,000
	Visit	14 (0.39)			15,159,734
Hospitalization	Consultation	8 (0.22)			2,023,500
	Para clinic	12 (0.34)			5,817,068
	Treatment	9 (0.25)			2,230,000
	Hoteling	14 (0.39)			44,135,400
	Other	13 (0.37)			6,242,211
Total					2,972,360,263

Table 3. The Estimation of Complication Cost of Leishmaniosis

Complication type	Group	N (%)	Practice	Appointment	Unit Cost (Rials)	Total Cost (Rials)
Heart, liver, kidney	>60 years	68 (1.9)	Medical examination	4	55,000	14,960,000
		68 (1.9)	Para clinic	4	157,200	10,689,600
		68 (1.9)	ECG	4	37,830	10,289,760
		68 (1.9)	Cardiac counseling	1	55,000	3,740,000
	History of chronic disease	15 (0.42)	Cardiac counseling	1	55,000	825,000
		15 (0.42)	Para clinic	4	39,300	2,358,000
		15 (0.42)	ECG	4	37,830	2,269,800
Dermatology		157 (4.4)	Antihistamine	4*10	22,000	3,454,000
Drug side effects	> 60 and itraconazole	3 (0.08)	Para clinic	1	33,600	50,400
	Dapson	15 (0.42)	Para clinic	8	265,600	3,984,000
Depigmentation	Cryotherapy	356 (10)	Sunscreen	1	60,000	21,360,000
Infection	Head & neck & limb	3060 (86)	Local dressing	10	21,800	667,080,000
	Infected wound	72 (2)	Cephalexin	4*10	32,000	2,304,000
Scar		18 (0.5)	Laser therapy	3	300,000	16,200,000
		1	Plastic surgery	1	1,650,000	1,650,000
Total						750,924,800

incidence was 79 per 100,000 persons. Considering the occurrence of this disease during the 1356-1390 Persian years, which was 20 to 40 per 100,000 people (30), the incidence is much higher than the national levels (almost 2.5 times higher). Also compared with the annual incidence of leishmaniosis in Mashhad which is reported to be 17-106 per 100,000 persons from 1370 to 1389 (30), the findings of this study are in the middle of this spectrum. This increase can be caused by factors such as the increasing migrant population from village to town. This migrant population creates marginalized textures around the cities. The environmental and social conditions of this context can increase the prevalence of the disease. Among other factors is the urban population growth in the province, especially Mashhad—the rural-to-urban population ratio was 70 to 30 in 1360, which has changed to 30 to 70 nowadays. The increase in the urban population alone cannot be the reason for the increased incidence of this disease, but the increase in urban population without access to minimal required infrastructure will create areas that provide the proper conditions for the spread of disease. Another factor can be the tourist and pilgrim population of Mashhad (31): about 15 million tourists and pilgrims visit the city of Mashhad annually. Last but not least, the increased sensitivity of tests and improved diagnostic methods can be another factor that leads to increased incidence through higher case findings.

In other studies (32, 33) conducted in endemic areas, childhood was reported to be the most common age of infection. After this age, the disease incidence decreases due to acquired immunity (34, 35). The higher incidence of adolescents can be explained by the fact that this age group is mostly present in the open environment at night and is exposed to mosquito bites (36).

In this study, 15% of the suspicious patients had a second

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Table 4. The Estimation of Other Clinical Practices for Managing Leishmaniosis

	Clinical Practice	N (%)	Unit Cost (Rials)	Total Cost (Rials)
Recurrence of lesions	Clinical diagnosis	1068 (30)	85,000	90,780,000
	Laboratory diagnosis	1068 (30)	15,400	16,447,200
	Treatment	1068 (30)	812,100	867,322,800
	Drug side effects	51 (4.8)	524,500	26,749,500
	Wound complications	107 (10)	72,500	7,757,500
	Local dressing	919 (86)	218,000	200,342,000
Drug resistance	Clinical diagnosis	385 (10.8)	55,000	21,175,000
	Treatment	385 (10.8)	797,500	307,037,500
	Drug side effects	41 (10.6)	197,100	8,081,100
	Wound complications	8 (2)	32,000	256,000
	Local dressing	332 (86)	218,000	72,376,000
Other treatment and recovery problems	Third doctor's visit	712 (20)	55,000	39,160,000
	Local dressing	675 (95)	218,000	735,750,000
Total				2,385,144,300

Table 5. The cost of Various Health Care Measures for Leishmaniosis

Care measures	N (%)	Cost (Rial)
Clinical diagnosis	3558 (100)	301,704,000
Paraclinical diagnosis	3558 (100)	52,801,700
Treatment	3558 (100)	2,972,360,263
Dressing	3060 (86)	1,402,830,000
Clinical diagnosis (third round)	712 (20)	39,160,000
Drug side effects	142 (4)	52,620,560
Wound side effects	187 (5.3)	41,514,000
Recurrence of lesions	1068 (30)	1,209,399,000
Drug resistance	385 (10.8)	408,925,600
Disease surveillance	3558 (100)	1,800,000,000
Total		8,281,315,123

smear test, a few cases (5.5 per 100,000) had a lesion biopsy due to 2 suspicious smears, and rare cases (1 out of 100,000) were referred for performing the Leshman test. Because of the high experience and skill resulting from the large number of laboratory cases due to the endemicity of the disease in the region, the low frequencies of reexamination and performing supplementary tests can indicate the proficiency of the laboratory personnel in diagnosing smear cases.

The cost of treating cutaneous leishmaniosis per patient in different countries ranges from $300 to $1200 (37). In a study conducted in this field in Qom province between 2010 and 2012, the total cost for each patient was >2.5 million Rials. In the same study, the patient's out-of-pocket costs were calculated to be about 2.4 million Rials, and the average total cost of the treatment was estimated to be about 2.76 million Rials (38). The per capita cost of the disease in this study was 2.106 million Rials (equal to $210), which is less than the estimate of the Qom study (38). It should be kept in mind that in the Qom study, the cost of hospital supplies and equipment was also considered, which is equivalent to 5% of the total costs. Also, in the aforementioned study, 10% of the estimated costs related to electricity, water, telephone, and transportation costs were not included in our study.

In a study carried out in the city of Bam (39), the per capita cost of treating the disease for each patient was estimated to be $70. Considering the inflation rate, the estimated cost is lower than the estimate of our study. The creation of a centralized cutaneous leishmaniosis institute in the city of Bam, which was responsible for the diagnosis and treatment of diagnosed cases, and the fact that all services are gathered in 1 center may have reduced the cost of treatment. It seems that due to the endemic nature of the disease in Khorasan Razavi province and Mashhad and the high incidence of the disease, the establishment of specialized and integrative care centers to perform all diagnostic, treatment, and care services in these centers can be effective in providing high-quality care and reducing costs.

In the studies conducted in Peru and Guatemala, the per capita cost of cutaneous leishmaniosis was $300 and $280, respectively (40, 41). This was estimated to be $245 for Colombia (42). If we consider that each dollar is equivalent to 10,000 Rials (based on the dollar-rial exchange rate in 2012/2013), our cost would be $210, which is lower than the aforementioned countries.

In this study, the cost of clinical diagnosis of the disease was 301,704,000 Rials (84,796 Rials per capita), 30% of patients were visited by specialist doctors, and 70% of patients were visited by general doctors. Because of the high incidence of CL and the considerable gap between the cost of general physicians and specialists, 1 strategy could be empowering general physicians to perform the diagnosis and treatment of leishmaniosis patients and only a few cases that may not have responded to common treatments and require complex measures could be referred to the specialist doctor. In this case, a significant part of the cost of clinical diagnosis of the disease can be reduced and saved.

One of the main drugs used in the systemic and topical treatment of this disease is glucantime, the cost of administration and injection of this drug in this study was 2411 million Rials. Considering the high cost of prescription of this drug and on the other hand, the lack of domestic production of this drug in Iran, which makes it difficult to access it due to sanctions, the priority of investigating alternative drugs can be included in the list of research topics of

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the country's research centers.

Examining the list of drugs used in the treatment of CL in the form of systemic, topical, and physical treatment methods shows a great variety of treatment methods, which is in accordance with the frequencies declared by participating doctors in the expert panels of this study. It seems that the preparation of diagnostic and treatment guidelines for this disease based on the most reliable scientific evidence and taking into account national and regional requirements and facilities can create unanimity in the methods of diagnosis, treatment, and care of the disease and reduce the economic burden of the disease.

This study is not without limitations. We did not include intangible costs of CL since the aim of the study was to analyze the direct costs of CL. In addition, the study group was limited to 1 year. However, using the patients' data from the surveillance system of a large university in northeast Iran and considering all possible outcomes and treatment modalities using a comprehensive model were among the strengths of this study.

Conclusion

Considering the scarcity of resources that every health system encounters, especially in developing countries, the economic burden of 7.5 billion Rials (equal to $750,000) for a city with a population of 5 million is a considerable amount for the healthcare system. In addition to this, the indirect costs of the disease, such as the costs of the patient's disability, travel costs, and current costs in the health system, as well as the intangible costs of the disease such as suffering and pain of the patients, mental and psychological problems caused by lesions in the face and open areas of the body, et cetera, can enlighten the high burden of the disease. On the other hand, considering that the predisposing factors are avoidable by using less expensive and highly effective solutions, it is possible to reduce the occurrence of the disease and prevent its economic burden. Of course, it should be kept in mind that the plans and solutions to prevent this disease require cooperation between the various parts of the health sector as well as common understanding and agreement on this issue in other related sectors.

Authors' Contributions

Study design: M.K., M.N.N., M.Y.
Data Collection: M.N.N., M.Y.
Data analysis: M.K., M.N.N., A.K., M.K.R.
Drafting manuscript: M.K.R., A.K.
Critical revising; M.K., M.N.N., M.Y.,
Final approval: M.K., M.N.N., M.Y., A.K., M.K.R.

Ethical Considerations

The protocol of this study is registered and approved by the Vice Chancellor for Research at Mashhad University of Medical Sciences (ID: 910326) and the ethical committee of Mashhad University of Medical Sciences.

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Conflict of Interests

The authors declare that they have no competing interests.

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