scientific reports

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Residential environment, human behavior and socio-economic status in transmission of cutaneous leishmaniasis in central Iran

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Cutaneous leishmaniasis (CL) is a vector-borne disease occurred through the bite of sandflies. Due to impact of environmental factors on the disease, this study aimed to assess the association between socio-economic status (SES), domestic, peri-domestic, and human behavior factors and the transmission of CL in Isfahan province in central Iran. This case-control study was conducted from March 2021 till March 2022 on 322 participants. Cases and controls were selected among CL patients and people with no history of leishmaniasis respectively by cluster random sampling method in a ratio of 1:1. A semi-structured questionnaire was completed for each patient and control. Multiple logistic regression models and odds ratio (OR) estimator were used to assess the relationships. In final model after adjusting for potential confounders the variables "moderate social and economic status", "individuals who rest outside at night in summer", "the presence of animals near the residence" and also the variables related to distance of homes to gathering places of insects remained significant. Adults and individuals who use preventive measures such as insecticides, insect repellent pen and sleeping the mosquito net significantly decrease the risk of disease. Our findings showed that human behavior and peri-domestic factors have most effects on transmission of leishmaniasis.

Cutaneous leishmaniasis (CL) is a vector-borne disease transmitted to humans through the bite of infected sandflies[1,2]. Its reservoirs include wild or semi-domesticated animals, such as rodents (2, 3). The disease manifests in three main clinical forms: cutaneous, mucosal, and visceral leishmaniasis[2,3]. According to the World Health Organization (WHO), CL is one of the most significant tropical diseases[4,5]. Leishmaniasis affects regions in Americas, Asia, Europe, and Africa, with a growing global incidence[4,6]. More than 350 million people are at risk, and the annual global incidence of CL is estimated at 0.7–1.2 million new cases[1,7,8]. Over 90% of CL cases occur in eight countries: Afghanistan, Algeria, Brazil, Peru, Saudi Arabia, Syria, Iraq, and Iran[1,9]. In Iran, approximately 30,000 cases of CL are reported annually, with the disease being endemic in 17 provinces, particularly South Khorasan, Fars, Isfahan, Khuzestan, Kerman, Ilam, and Bushehr[10–12]. Isfahan province is a major hotspot for zoonotic cutaneous leishmaniasis (ZCL), reporting the highest incidence rates in the country[1,13].

The epidemiology of CL is influenced by environmental factors such as topography, and vegetation cover[3,14,15]. Socio-economic factors, such as education, economic status, and household size, are also linked to the disease[2,16,17]. Increased risk is associated with resting outdoors at night without protection and residing in rural or forest-adjacent areas[11,18]. Additionally, demographic characteristics like age and gender play a role, with males being more exposed due to outdoor activities[19,20]. Domestic risk factors including houses with cracked walls, number of inhabitants, and history of CL infection in household's members and also residing close to a forest or to sights of wild rodents as outdoor risk factors were associated with high risk of CL[21]. These findings emphasize the complex interplay of residential environmental, socio-economic, and demographic factors in CL epidemiology, underscoring the need for integrated prevention and control strategies. Given that few studies have investigated the effect of residential environmental factors on the incidence of CL in Iran. Therefore, the aim of this study was to assess the association between socioeconomic status (SES), domestic, peri-domestic,

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and human behavior risk factors with the transmission of cutaneous leishmaniasis in Isfahan province in the center of Iran.

Methods

Study area

Isfahan Province in central Iran consists of 44 counties with an area of 115,932 km^2 lying within the 31°43′ to 34°22′ N and 49°38′ to 55° 31′ E. It has a moderate and dry climate and is considered as an arid and semiarid region of the Iran with a population of approximately 4,629,312 inhabitants. All the districts where cutaneous Leishmaniasis was endemic including Isfahan, Ardestan, Borkhar, Tiran and Karvan, Chadegan, Khansar, Khomeinishahr, Khoor and Biabanak, Dehaghan, semirom, Shahinshahr and Meimeh, Shahreza, Fereidan, Fereidoonshahr, Falavarjan, Golpaigan, Lenjan, Mobarakeh, Naein, Natanz and Najafabad were included in our study.

Participants and study design

This is a case-control study that cases were sampling patients who were diagnosed as cutaneous leishmaniasis from March 2021 till March 2022 and clinically and paraclinicaly were confirmed in the communicable diseases control unit of Isfahan provincial health center. Cases were selected from the epidemiologic data forms of this disease. The cluster random sampling method was applied to select the patients based on the recorded data. We divided our study population to clusters according to the residential location. Then we randomly selected the samples based on proportion assigned to any location. The control group was selected from people who lived in the neighborhood of the case group and had no history of leishmaniasis in a ratio of 1:1. In this way, the controls were selected by using the sequence of phone numbers of the case group whose information was obtained from the health centers of the province. After the phone call, if respondent had a history of leishmaniasis, its phone number was removed and replaced by the next number. Both cases and controls should be resided more than one year. In total, 322 participants were enrolled in this study with response rate of 94.7%.

Data collection

A semi-structured questionnaire consisted of potential risk factors categorized into four groups for purposes of analysis: demographic and economic factors, factors related to human behavior, factors related to indoor dwelling environment, and factors related to outdoor environment was completed for each patient and control. Reliability was estimated using internal consistency and face validity was approved by expert panel. The questionnaire was pre-validated in previous study by Nilforoushzadeh et al.[22]. Data collection was performed by a trained health worker and by interviewing. To prevent information bias, the purpose of the study, working place of the questioner and the purpose of data collection were explained to the participants.

Ethical consideration

The methods were carried out in accordance with guidelines and regulations, and also protocols were approved by National Institute for Medical Research Development of Iran (No. 228289). Informed consent was obtained from all participants and/or their legal guardian(s) in this study.

The questionnaire consisted of following questions: sex, age (children aged 0–5 years, teenagers aged 6–19 years, and adults aged 20 years and above), education (primary/secondary, higher secondary, higher education/university), number of people living in the house, residence place, number of people who are working, situation of a person's activity being either rural or urban, occupation, the average time spending out of home, number of nights spending in working place, number of days or hours pending out of home for walking (hours in a day), hours spending in farm for working (in case of being a farmer), source of water supply, sewage disposal system, sleeping under mosquito net, sleeping out of home (number of nights), using insecticide in a month, using insect replants in a month, type of windows, using curtain in front of windows and doors, material used to construct walls and roofs, number of rooms, number of people in bedroom, distance of river from house, distance of farms from house, keeping pets in houses, animals around the house, distance of water sources from house, kind of water supply in house, using protection to avoid insects. Data for socio-economic status were also obtained by a multidimensional tool consisted the social and economic status[23,24]. The indicators evaluated in SES included education level, occupation, income level, wealth and place of residence[25,26]. First, we obtained the scores of SES indicators for each participant and then multiplied with their weight based on our previous study[27]. The sum of the individual scores was categorized into 5 groups, from the lowest "100" to the highest "720" in which, standardized to "0-100" quintile of the final scores included extremely poor "0 to 19.9", poor "20-39.9", moderate "40-59.9", good "60-79.9" and wealthy "80–100" classes[27].

Statistical analysis

To assess the correlation between categorical variables, chi-square test was used. Multiple logistic regression models were used to evaluate relationships between risk factors and leishmaniasis by accounting odds ratios (OR) with 95% confidence intervals. Covariates identified in data base as potential confounders included in the multiple-adjusted models. Data were analyzed by STATA 17 software (Stata Corporation, College Station, Texas).

Results

Descriptive analysis

A total of 322 participants recruited for our study. Males constituted 66.46% of the cases and 59.63% of the controls. The majority of both cases (75.78%) and controls (91.31%) were adults. Among the cases, 70.81% had

higher /university education. Regarding socio-economic status (SES), scores were calculated based on Table 1 by multiplying the individual scores by their respective weights. The resulting sums were categorized into relevant groups. Due to the limited number of participants classified as "extremely poor" or "wealthy," we consolidated the SES categories into three levels: "poor," "moderate," and "good." In this classification, 44.30% of the cases and 35.66% of the controls fell into the "poor" category. The most common occupation among cases was being a student (25.47%), whereas among controls, it was self-employment or freelance work (23.60%). A significant proportion of cases (62.3%) reported sleeping outside their homes, compared to 29.56% of the controls. Among the cases, 41.03% used some form of protection to avoid insect contact with the skin, compared to 51.25% of the controls. Regarding the use of mosquito nets, 25% of cases and 51.55% of controls reported owning and sleeping under a mosquito net every night.

A higher proportion of controls (71%) used insecticides, while 19.38% of cases and 55.28% of controls reported using insect repellents. The presence of animals around homes was notably more common among cases (68.75%) than controls (13.88%).

Further details of the results are provided in Table 2.

Risk factor analysis

Table 2 presents the distribution of cases and controls, along with the corresponding crude and adjusted odds ratios (ORs) for the variables analyzed across the four group models.

In Category A, under "adults," the disease occurrence was significantly lower compared to other age groups (OR = 0.18; 95% CI: 0.02–1.56). Additionally, individuals categorized as having a "poor socio-economic status" (OR = 1.77; 95% CI: 0.99–3.16) demonstrated a significant association with the disease in the crude model. The variable "sex" did not show a significant association with the disease. After adjusting for other factors in the multivariable models, the disease prevalence remained significantly lower among "adults" (OR = 0.18; 95% CI: 0.02–1.56) and "women" (OR = 0.17; 95% CI: 0.05–0.53). However, individuals with a "poor socio-economic status" exhibited a significantly increased risk of disease (OR = 1.87; 95% CI: 1.03–3.42) (Table 2).

In Category B, which includes factors related to human behavior, five of the six analyzed factors were statistically significant. "Individuals who preferred spending the night at their workplace" (OR = 2.03; 95% CI: 1.26–3.25) and "individuals who preferred resting outside at night during summer" (OR = 3.89; 95% CI: 2.44–6.22) were significantly associated with the disease in the crude model. Protective factors included "using a mosquito net" (OR = 0.31; 95% CI: 0.19–0.50), "use of indoor insecticides" (OR = 0.22; 95% CI: 0.14–0.36), and "using an insect repellent pen" (OR = 0.19; 95% CI: 0.12–0.32). The variable "average time spent outside the home" did not show a significant association with the disease.

After adjustment for other factors in the multivariable models, the protective factors that remained statistically significant included "using an insect repellent pen" (OR = 0.36; 95% CI: 0.19–0.67), "use of indoor insecticides" (OR = 0.39; 95% CI: 0.21–0.70), and "using a mosquito net" (OR = 0.32; 95% CI: 0.18–0.57). Conversely, "spending the night at the workplace" (OR = 1.97; 95% CI: 1.11–3.49) and "resting outside at night during summer" (OR = 3.22; 95% CI: 1.83–5.67) remained significantly associated with the disease (Table 2).

Two of the four factors classified under category C, which pertains to domestic characteristics, demonstrated statistical significance in the crude model. These factors included "Installing nets at entrances" (OR = 0.34; 95% CI: 0.20–0.56) and "Keeping pets in houses" (OR = 5.33; 95% CI: 2.27–12.5). After adjusting for other variables in the multivariable models, both factors remained statistically significant: "Installing nets at entrances" (OR = 0.41; 95% CI: 0.23–0.71) and "Keeping pets in houses" (OR = 4.53; 95% CI: 1.89–10.82) (Table 2).

In Category D, all five factors related to the outdoor environment were found to be significant in the crude model. These factors included: (1) the use of wells for water supply, (2) the presence of animals around the house, (3) a distance of less than 200 m from agricultural or barren lands and livestock areas, (4) a distance of less than 150 m to wells and springs, and (5) the use of wells for sewage disposal. After adjusting for other variables in the multivariable model, only two factors remained significant: the presence of animals around the house (OR = 7.11; 95% CI: 3.55–14.21) and the use of wells for sewage disposal (OR = 2.8; 95% CI: 1.08–7.22) (Table 2).

In the final model, nine factors remained significant after controlling for all variables. The significant risk factors were: (1) moderate socioeconomic status (OR_moderate/poor = 2.8; 95% CI: 1.06–7.36), (2) individuals resting outside at night during summer (OR_yes/no = 3.84; 95% CI: 1.78–8.26), (3) the presence of animals near the residence (OR_yes/no = 3.69; 95% CI: 1.31–10.43), (4) a residence located less than 200 m from agricultural or barren lands and livestock areas (OR_under 200 m/above 200 m = 4.05; 95% CI: 1.47–11.16), and (5) a residence located less than 150 m from wells and springs (OR_under 150 m/above 150 m = 2.64; 95% CI: 1.05–6.67).

Additionally, several factors were identified as significantly protective. These included: (1) belonging to the adult age group (OR_adult/child = 0.03; 95% CI: 0.003–0.22), (2) sleeping under a mosquito net (OR_yes/no = 0.24; 95% CI: 0.10–0.57), (3) using insecticides (OR_yes/no = 0.39; 95% CI: 0.16–0.95), and (4) using insect

No.	Indicator	Weight	Impact on SES
1	Income	4.5	30
2	Occupation	4.0	27
3	Education	3	20
4	Home status	2.0	13
5	Family size	1.5	10

Table 1. The average weight and the percentage of impact on SES[37].

Variables	Controls $N=161$ N (%)	Cases $N=161$ N (%)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)
A. Demographic and economic factors[a]				
Age				
Child	4 (2.48)	17 (10.56)	1	1
Teenager	10 (6.21)	22 (13.66)	0.52 (0.14–1.9)	0.55 (0.14–2.09)
Adult	147 (91.31)	122 (75.78)	**0.18 (0.06–0.56)**	**0.17 (0.05–0.53)**
Sex				
Male	96 (59.63)	107 (66.46)	1	10.53 (0.11–2.5)
Female	65 (40.37)	54 (33.54)	0.75 (0.47–1.17)	**0.59 (0.36–0.96)**
Socio-economic status				
Poor	56 (35.66)	70 (44.30)	**1.77 (0.99–3.16)**	**1.87 (1.03–3.42)**
Moderate	57 (36.31)	57 (36.08)	1.42 (0.79–2.56)	1.35 (0.73–2.49)
Good	44 (28.03)	31(19.62)	1	1
Variables	**Controls** N (%)	**Cases** N (%)	**Crude OR (95% CI)**	**Adjusted OR[b,c,d] (95% CI)**
B. Factors related to human behavior[b]				
The average time spending out of home				
< 4 h	29 (18.35)	29 (18.24)	1	1
≥ 4 h	129 (81.65)	130 (81.76)	1.01 (0.57–1.78)	0.72 (0.35–1.49)
Spending the night in working place				
No	114 (72.61)	89 (56.69)	1	1
Yes	43 (27.39)	68 (43.31)	**2.03 (1.26–3.25)**	**1.97 (1.11–3.49)**
Using insect repellent pen				
No	72 (44.72)	129 (80.63)	1	1
Yes	89 (55.28)	31 (19.38)	**0.19 (0.12–0.32)**	**0.36 (0.19–0.67)**
Use of indoor insecticides				
No	45 (28.13)	102 (63.75)	1	1
Yes	115 (71.88)	58 (36.25)	**0.22 (0.14–0.36)**	**0.39 (0.21–0.7)**
Using a mosquito nets				
No	78 (48.45)	117 (75.00)	1	1
Yes	83 (51.55)	39 (25.00)	**0.31 (0.19–0.50)**	**0.32 (0.18–0.57)**
Resting outside at night in summer				
No	112 (40.44)	60 (37.97)	1	1
Yes	47 (29.56)	98 (62.30)	**3.89 (2.44–6.22)**	**3.22 (1.83–5.67)**
C. Domestic characteristics[c]				
Installing nets at entrances				
NO	30 (18.63)	64 (40.25)	1	1
Yes	131 (81.37)	95 (59.75)	**0.34 (0.20–0.56)**	**0.41 (0.23–0.71)**
Keeping pets in houses				
NO	154 (95.65)	128 (80.50)	1	1
Yes	7 (4.35)	31 (19.50)	**5.33 (2.27–12.50)**	**4.53 (1.89–10.82)**
Number of rooms				
0–1	27 (16.88)	41 (25.79)	1	1
≥ 2	133 (83.13)	118 (74.21)	0.58 (0.34–1.01)	0.79 (0.43–1.44)
Suitable for ceiling and wall materials				
No	8 (4.97)	15 (9.38)	1.98 (0.81–4.81)	1.13 (0.43–3.02)
Yes	153 (95.03)	145 (90.63)	1	1
D. Peri-domestic characteristics[d]				
Source of water supply				
Well system	6 (3.73)	19 (11.80)	**3.46 (1.34–8.9)**	1.17 (0.37–3.73)
Urban system	155 (96.27)	142 (88.20)	1	1
Presence of animals around the house				
No	133 (83.13)	50 (31.25)	1	1
Yes	27 (16.88)	110 (68.75)	**10.84 (6.37–18.45)**	**7.11 (3.55–14.21)**

Continued

Variables	Controls	Cases	Crude OR (95% CI)	Adjusted OR[b,c,d] (95% CI)
	N (%)	*N* (%)		
Distance to agricultural and barren lands and places with livestock				
Under 200 m	45 (27.95)	100 (62.11)	**4.23 (2.64–6.75)**	1.3 (0.69–2.45)
Above 200 m	116 (70.05)	61 (37.89)	1	1
Distance to well and springs				
Under 150 m	26 (16.15)	69 (42.86)	**3.89 (2.31–6.57)**	1.26 (0.64–2.49)
Above 150 m	135 (83.85)	92 (57.14)	**1**	1
Wastewater				
Well system	9 (4.97)	44 (28.39)	**7.58 (3.43–16.74)**	**2.8 (1.08–7.22)**
Urban system	153 (95.03)	111 (71.61)	1	1

Table 2. Analysis of the factors associated with cutaneous leishmaniasis in Isfahan. [a]Variables related to demographic and economic factors (Age, Sex, Socio-economic status) were entered into the model. [b]Variables related to human behavior (the average time spending out of home, Spending the night in working place, using insect repellent pen, Use of indoor insecticides, Using a mosquito nets, resting outside at night in summer) were entered into the model. [c]Variables related to domestic characteristics (Installing nets at entrances, Keeping pets in houses, Number of rooms, Suitable for ceiling and wall materials) were entered into the model. [d]Variables related to Peri-domestic characteristics (source of water supply, Presence of animals around the house Distance to agricultural and barren lands and places with livestock, Distance to well and springs, Wastewater) were entered into the model. Significant values are in bold.

Variable	Adjusted odds ratio[a]	95% CI	*P*-value
Adult age group	0.03	0.003–0.22	$P<0.001$
Moderate social and economic status	2.8	1.06–7.36	0.037
The presence of animals near the residence	3.69	1.31–10.43	0.014
Distance the residence less than 200 m from agricultural and barren lands and places with livestock	4.05	1.47–11.16	0.007
Distance the residence less than 150 m to the well and springs	2.64	1.05–6.67	0.040
Individuals who rest outside at night in summer	3.84	1.78–8.26	$P<0.001$
Individual who sleeps under mosquito net	0.24	0.10–0.57	$P<0.001$
Individual who uses insecticide	0.39	0.16–0.95	0.037
Individual who uses insect repellent pen	0.13	0.05–0.36	$P<0.001$

Table 3. Final model showing adjusted odds ratios and 95% confidence intervals for factors related to cutaneous leishmaniasis in Isfahan. [a]Remained significant variables related to all socio-economic, human behavior, domestic and peri-domestic characteristics were entered into the model.

repellent pens (OR_yes/no = 0.13; 95% CI: 0.05–0.36). The odds ratios for these associations are summarized in Table 3.

Discussion

The residential environment plays a key role on the transmission of leishmaniasis, especially since the biomedical research has not yet achieved definitive findings on the control of leishmaniasis[28,29]. Housing conditions, peri-domestic characteristics and human behavior are the main factors of residential environment in occurrence of the disease[29].

In this study, children and in final model the adults were found to be more affected by the disease compared to other age groups. Additionally, a high proportion of participants involved with leishmaniasis were males. This is consistent with most of studies for sex, may be because of job activities and spending more time outside of home and habits of wearing clothes[30–32]. While leishmaniasis occurs across all age groups in endemic areas, it predominantly affects children[33,34]. However in some studies, adults were included in the vulnerable age group[32,35]. This finding is in agreement with our study.

Poverty as one of the main risk factor can increase leishmaniasis, and the previous studies showed that the higher rate of poverty has caused a higher incidence of leishmaniasis[2,36,37]. In the present study as well as most other studies, individuals with the level of "poor socio-economic status" had significant association with disease. However in the final model, after controlling for all factors, "moderate social and economic status" was remained significant. Because the cases and controls were obtained from common places, although the relationship was significant, there was not much difference between the two groups.

Many studies have discussed the effect of control measures to protect and prevent the transmission of leishmaniasis[22,29,38], although in a study by Lehlewa[29], the preventive measures, such as the use of bed net couldn't decrease the odds of having CL.

Our study was consistent with most previous studies[22,38], so that it showed that the protective factors included "using insect repellent pen", "use of indoor insecticides", "using mosquito nets" were statistically significant. Factors such as "spending the night in working place" and "resting outside at night in summer" were associated with the disease as the risk factors. However, the adoption of these measures is often limited by cultural practices.

Indoor characteristics have always been important factors in the transmission of leishmaniasis[22,29,39]. "Installing nets at entrances" and "keeping pets in houses", the protective and risk factors respectively, were statistically significant. Other studies indicated the correlation of animal caring with the risk of leishmaniasis, through presence of domestic animals[39,40]. Reithinger[41] in their study illustrated that materials used in construction and number of rooms or windows per people inside the house can significantly affect leishmaniasis risk in Kabul. In terms of these two factors, this is contrary to our results. Although more density of household members and improper materials in home construction could increase sand flies' exposure, but in our study area, this problem can be solved because of the small size of family and the large area of the house (in terms of economic status). In final model, none of the domestic variables remained significant.

In the present study, peri-domestic factors including "the use of wells for sewage" and in final model "the presence of animals near the residence areas", "distance the residence less than 200 meters from agricultural and barren lands and places with livestock", "distance the residence less than 150 meters to the well and springs" were significantly associated with CL.

In line with our study, many authors have addressed peri-domestic factors such as relationship between "presence of animals in peri-domestic areas" or "proximity of houses to water sources" and leishmaniasis in their research[22,39,42,43]. Improper waste management and stagnant water sources near residential areas and also proximity to rivers attract sandflies[44].

WHO guidelines[8], illustrated that the identification of animal burrows and sources of food for them can be useful for control measures. Also, poisoning and bed nets considered as protective measures against leishmaniasis transmission.

In our study peri-domestic factors and human behavior had the most impact on transmission of CL. It seems that this is because the individuals living near agricultural fields or livestock may adopt behaviors that inadvertently increase their risk, such as frequent outdoor activity or close contact with animals.

Limitation

Due to the limitation in classification of the factor "suitability of the roof and floor of the house" caused by the non-cooperation of some participants, the residential confounder distorted the relationship between exposure and outcome and it was a disadvantage of our study. Also, due to the possibility that respondents may not recall events accurately in the human behavior section, we suffered information bias, which because of same probability of making the error in both study groups, the non-differential misclassification bias was expected.

Conclusion

Our findings showed that human behavior including use of insecticides and spending nights outside, and also peri-domestic factors including the presence of animals, agricultural and barren lands, places with livestock, well and springs near the residence areas have most effects on transmission of leishmaniasis. Residential environmental management in polluted areas near the homes and promoting protective behaviors can protect people who live in endemic areas.

Data availability

The data used in this study are available upon request by contacting the corresponding author (M.R.M) mrmaracy@yahoo.co.uk.

Received: 4 February 2024; Accepted: 25 February 2025
Published online: 01 March 2025

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Acknowledgements

We gratefully acknowledge the contribution of patients and people to participate in this research and also National Institute for Medical Research Development of Iran.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis

were performed by A.H., S.M., N.M. and M.R.R. The first draft of the manuscript was written by N.M. and A.H. and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding
This work was supported by grant of National Institute for Medical Research Development Islamic Republic of Iran (Electronic Application No. 228289).

Declarations

Competing interests
The authors declare no competing interests.

Additional information
Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-91999-6.

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