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Environmental and climatic risk factors of human cystic echinococcosis in the northeast of Iran

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Abstract

Cystic echinococcosis (CE) is a significant zoonotic helminthic disease with considerable public health and economic impact in endemic regions. We aimed to analyse the climatic and environmental factors affecting the human CE cases in North Khorasan Province, northeast Iran. Using a geographic information system, we map the addresses of 316 hospitalised CE patients from 2012 to 2022 and examined the influence of climatic variables, altitude, and land cover on CE case distribution. Data were analysed using logistic regression models. Most patients were female (58.9%) and aged 21–60 years (67.4%), with liver involvement being the most common (57.3%). The multivariate model identified urban settings, irrigated and dry farms, soil temperature, and humidity as the most important geoclimatic determinants, respectively. In contrast, gardens, moderate and excellent rangelands, minimum, maximum, and mean air temperatures, and rainfall were only found to be significant factors in univariate models. High-risk areas for CE include urban and suburban regions, surrounding fields, and pastures where stray dogs and wild canids roam, livestock husbandries are present, and residents consume unsanitised vegetables. Additionally, areas with lower soil and weather temperatures and higher humidity conditions that may enhance the survival of *E. granulosus* eggs dispersed by canids were identified as high-risk zones. Health managers can use these findings to prioritise control programs and allocate limited resources to these areas, ultimately reducing the future incidence of CE.

Introduction

Human cystic echinococcosis (CE), called hydatidosis or 'cystic hydatid disease', is a major zoonotic disease affecting people worldwide. It is caused by the larval stage of the dog tapeworm, which is part of the Echinococcus granulosus (*E. granulosus*) sensu lato complex (Gholami *et al.* 2018; Shafiei *et al.* 2019). This parasitic infection is particularly prevalent in impoverished regions and is often associated with herding communities that maintain large populations of grazing sheep (Ebrahimipour *et al.* 2020; Khalkhali *et al.* 2018). For *E. granulosus* to live, it needs definitive hosts, which dogs (both owned and stray) and other carnivores are. The adult worm lives in the proximal part of the host's intestine. A broad spectrum of mammals, including humans, goats, sheep, pigs, and cattle act as intermediate hosts. What makes the disease spread differently are the types and strains of *E. granulosus*, the number of intermediate host species that are available in different places, and other natural and artificial factors (Karamian *et al.* 2017; Shafiei *et al.* 2016).

Human infection typically occurs via the faecal-oral route by accidentally ingesting *E. granulosus* sensu lato (s.l.) eggs found in contaminated food, water, or soil, leading to the development of hydatid cysts in various anatomical organs (e.g., liver, lungs, spleen, heart). CE is responsible for significant morbidity and mortality among affected individuals (Neumayr *et al.* 2013). The clinical manifestations of CE can vary widely; some individuals may remain asymptomatic for extended periods, while others may experience symptoms after an incubation period lasting several months to years (Ebrahimipour *et al.* 2016; Fasihi Harandi *et al.* 2012). The severity of symptoms depends on factors such as the number and size of cysts, their developmental status (active or inactive phases), the specific organ involved, the localisation of the cysts within that organ, and the host's immune response. While some cases of CE can be effectively managed through chemotherapy or a watch-and-wait approach, more severe instances may require surgical intervention to alleviate associated complications (Firouzeh *et al.* 2021; Shafiei *et al.* 2024).

The prevalence and incidence of CE in endemic regions depend on several factors, including the presence of free-roaming dogs, dog ownership practices, conventional livestock husbandry and agriculture, close contact between people and animals, traditional home slaughtering practices without health oversight, and ecological and climatic variability (Borhani *et al.* 2020; Ghatee *et al.* 2020).

Geospatial data studies utilising maps or geographic information systems (GIS) provide reliable estimates of trends and distributions, offering valuable insights into disease frequency in specific geographic locations and predictions of disease patterns in regions lacking baseline data (Cromley 2003; Kanannejad *et al.* 2020). GIS has a lot of potential to help us learn more about parasitic diseases, like how environmental and climatic factors affect the spread of diseases, the host-parasite biogeography, clustering patterns, host distribution, and the risk of infection in hosts (Fakhar *et al.* 2017; Ghatee *et al.* 2018).

Limited GIS-based studies have evaluated human CE in various parts of Iran. North Khorasan province is one of the highest endemic areas for CE, with a notable human infection rate in northeastern Iran (Shafiei *et al.* 2021). However, GIS analyses have not been employed to study CE distribution or the role of key geoclimatic factors affecting CE in this region. Therefore, this study focuses on surgically managed CE cases and highlights effective geoclimatic risk factors that can be considered for future control programs.

Materials and methods

Study area

North Khorasan Province covers 28,434 km^2 of surface area and is located in northeast Iran with a steppe climate. The capital of the province is Bojnord city. This province comprises Bam and Safiabad, Bojnord, Esfarayen, Farouj, Garmeh, Jajarm, Maneh, Raz and Jargalan, Samghalan, and Shirvan (Figure 1). This area is one of the leading centres of animal husbandry, with many livestock, including sheep, cattle, goats, and camels in Iran, where many cases of human hydatidosis have been reported.

Data collection

This survey consisted of the data from 316 hospital records of echinococcosis patients from 2012 to 2022 who were treated for confirmed hydatidosis at hospitals in North Khorasan province. Ethics approval was granted by the Research Ethics Committee at the North Khorasan University of Medical Sciences (Approval ID: IR.NKUMS.REC. 1400.070, with Reg. No. 990171, Approval date: 2021-06-15).

Geospatial data

The hydatidosis patients' residences, according to the latitudes and longitudes of the villages and cities from which the patients come, were recorded on the city/village point shapefile map of North Khorasan province. The digital elevation model (DEM) raster layer

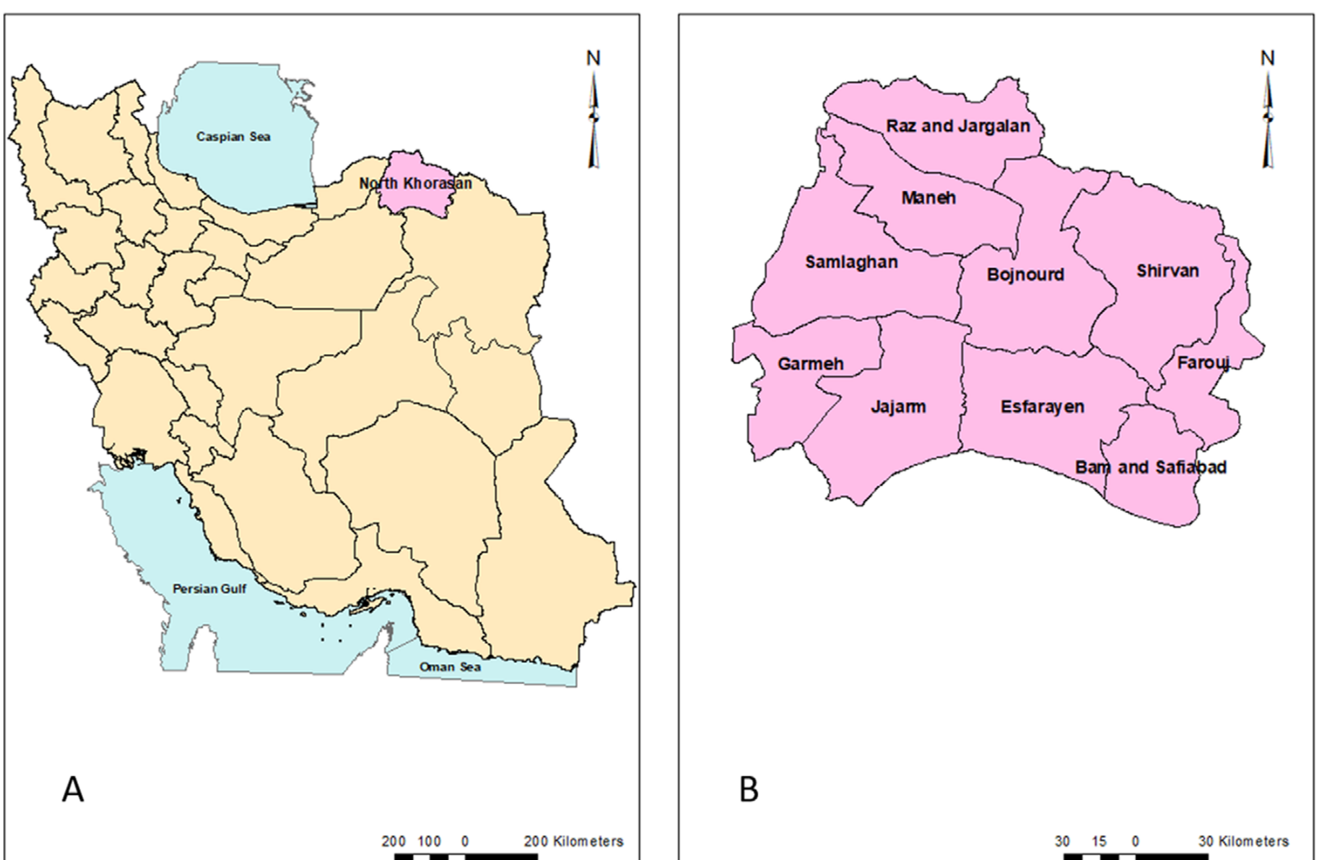

Figure 1. A, Iran map and North Khorasan location; B, North Khorasan province and its counties.

and the province and land cover vector layers were obtained from the Department of Natural Resources in North Khorasan province. For the study time, data from seven synoptic meteorological stations were acquired from the North Khorasan Province Weather Bureau, including weather temperatures, soil temperature, rainfall, humidity data, and the frequencies of frosty days. From these data, the mean annual temperature (MAT), maximum mean annual temperature (MaxMAT), minimum mean annual temperature (MinMAT), mean annual soil temperature (MAST), mean annual rainfall (MAR), mean annual humidity (MAH), and mean annual frequency of frosty days (MAFD) were calculated. After evaluating the accuracy of various interpolation methods using root-mean-square error (RMSE) and manual validation with training/test data, the spline interpolation model was used to make the annual iso-thermal, iso-hydral, and iso-humid layers. The Kriging interpolation method was then used to make the iso-frosty days raster layer, which had a resolution grid of 1 km × 1 km.

Geospatial analysis

All geospatial analysis was done by ArcGIS version 10.5 (http://www.esri.com/arcgis). The cities and villages point shape file layer was extracted with all raster layers. The identity tool was used to compute the geometric intersection of the layer obtained from extracting all raster layers with land cover (polygonal) vector layers to develop the final layer in which each point represented properties of all the overlapped identity features from the above-mentioned raster and vector layers. All maps were provided by current research team by layout tools using ArcMap from ArcGIS 10.5.

Statistical analysis

The attribute table of the final layer was exported to an Excel sheet for statistical analysis. Following the spatial characterisation of hydatidosis patients in North Khorasan province, we analysed the correlation between the disease and the dependent geoclimatic variables. Accordingly, using univariate and multivariate logistic regression models, the effect of environmental and climatic factors on the disease occurrence was investigated between residential points, including hydatidosis-reported and non-reported villages and cities. Prior to multivariate analysis, independent variables were checked for collinearity by pairwise correlation and variance inflation factor (VIF). The statistical analyses were performed using SPSS version 21.

Results

Hydatidosis was reported from 144 (6.1%) city/village areas from 2210 residential area points in the province. Most of the patients were female (59%), and they were in the 21–60 age range. 96.5% of cysts were from the liver and lung. The brain (1.2%) and right kidney (0.6%) were in the next levels, and other organs had only 2% of cysts (Table 1).

Table 1. The demographic data and frequency involved organs of patients in the studied area

Variable		Frequency	Percent
Gender	Female	186	58.9
	Male	130	41.1
Age	0–10	16	5.1
	11–20	48	15.2
	21–60	213	67.4
	> 60	39	12.3
Involved organ	Liver	181	57.3
	Lung	124	39.3
	Brain	4	1.3
	Right kidney	2	0.6
	Liver/lung	1	0.3
	Gallbladder	1	0.3
	Abdomen	1	0.3
	Peritoneum	1	0.3
	Pelvic	1	0.3

Univariate analysis

Climatic factors

Climatic analysis showed that weather temperature models, including MAT, MinMAT, MaxMAT, and MAST were significantly associated with the occurrence of hydatidosis in the current study (Figure 2). Accordingly, the chance of hydatidosis decreases 16%, 11%, 17%, and 26%, respectively, when temperature increases one centigrade degree for each model. MAR and MAH were significantly associated with the occurrence of hydatidosis in this province, where an increase of each millilitre of rain and humidity percent increases the chance of diseases close to 1% and 8%, respectively. In contrast, disease occurrence was not affected by MAFD (Table 2) (Figure 3).

Geographic factors

Among the different types of land, the surface area of the province's urban setting was the best predictor of hydratases. Living in cities raises the risk of getting diseases by 200 times. Gardens, irrigated farms, rain-fed farms, and moderate and good rangelands were other geographical determinants of disease, respectively. Forests and bare lands were not associated with disease in the study area. Altitude based on the DEM also was not associated with hydatidosis distribution in the North Khorasan Province (Table 3) (Figure 4).

Multivariate analysis

Severe collinearity was shown between MAT/MinMAT and MAT/-MaxMAT variables, so MAT was not included in the multivariate model. The other factors that affected the occurrence of hydatidosis in the univariate model were added to the multivariate model to see how these factors worked together. It was found that living in a city was the most significant factor affecting hydatidosis in the province. Irrigated and dry farms were other significant geographical determinants of disease in this model. MAST and MAH were the climatic factors shown to be effective on the hydatidosis occurrence in this model, while MAR, MinMAT, and MaxMAT were not significantly associated with the disease (Table 4).

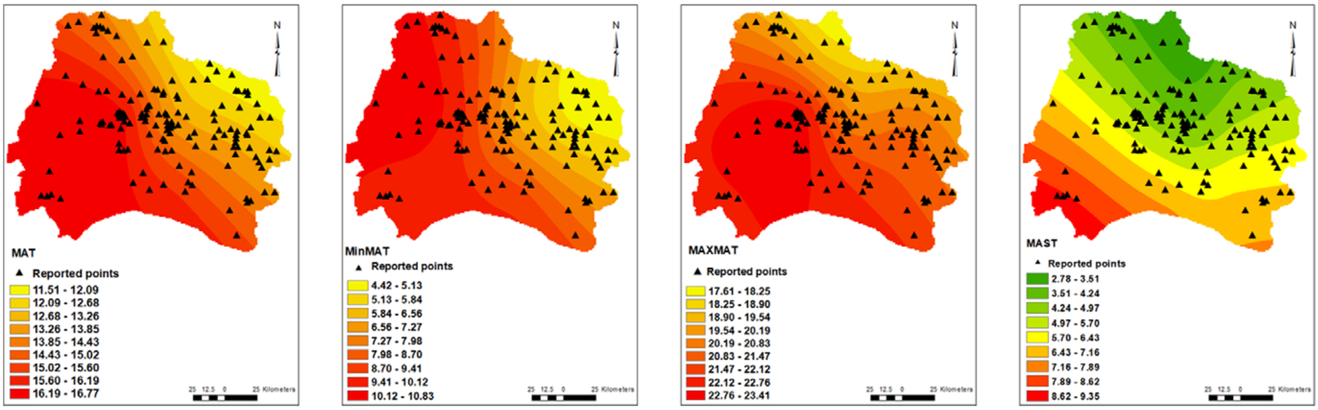

Figure 2. Points with CE were shown by a triangle symbol. Maps were created with ArcMap from ArcGIS 10.5. MAT = mean annual temperature; MinMAT = minimum mean annual temperature; MaxMAT = mean annual maximum temperature; MAST = mean annual soil temperature.

Table 2. Univariate analysis of climatic factors studied on the distribution of hydatidosis in North Khorasan province

Factors	P value	OR	CI
MAT	**0.004**	0.84	0.746–0.945
MinMAT	**0.017**	0.892	0.811–0.98
MaxMAT	**0.007**	0.836	0.734–0.953
MAST	**< 0.001**	0.674	0.586–0.775
MAR	**< 0.001**	1.007	1.003–1.011
MAH	**< 0.001**	1.081	1.052–1.112
MAFD	0.097	0.993	0.984–1.001

MAT = mean annual temperature; maximum MAT = maximum mean annual temperature; minimum MAT = minimum mean annual temperature; MAST = mean annual soil temperature; MAR = mean annual rainfall; MAH = mean annual humidity; MAFD = mean annual frequency of frosty days.

Table 3. Univariate analysis of geographic factors studied on the distribution of hydatidosis in North Khorasan province

Factors	P value	OR	CI
DEM	0.319	0.999	0.999–1.0001
Poor rangeland (constant)	0.000		
Moderate and good rangeland	**0.009**	4.267	1.429–12.741
Thin and semi dense forest	0.979	0.971	0.107–8.797
Garden	**0.031**	6.875	1.198–39.453
Dry (rained) farm	**0.002**	5.756	1.924–17.215
Irrigated farm	**0.001**	6.016	2.190–16.524
Urban area	**< 0.001**	200.357	53.434–751.258
Bareland and water areas	0.999	0.000	0.000

DEM = Digital elevation model.

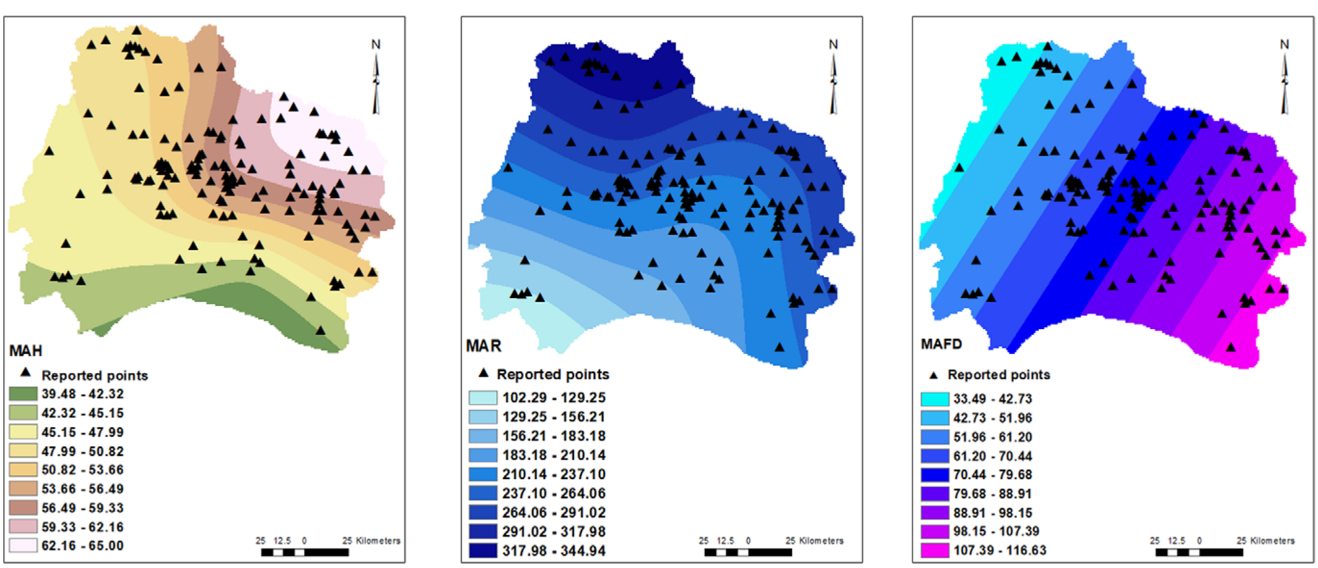

Figure 3. Points with CE were shown by a triangle symbol. Maps were created with ArcMap from ArcGIS 10.5. MAH = mean annual humidity; MAR = mean annual rainfall; MAFD = mean annual frequency of frosty days.

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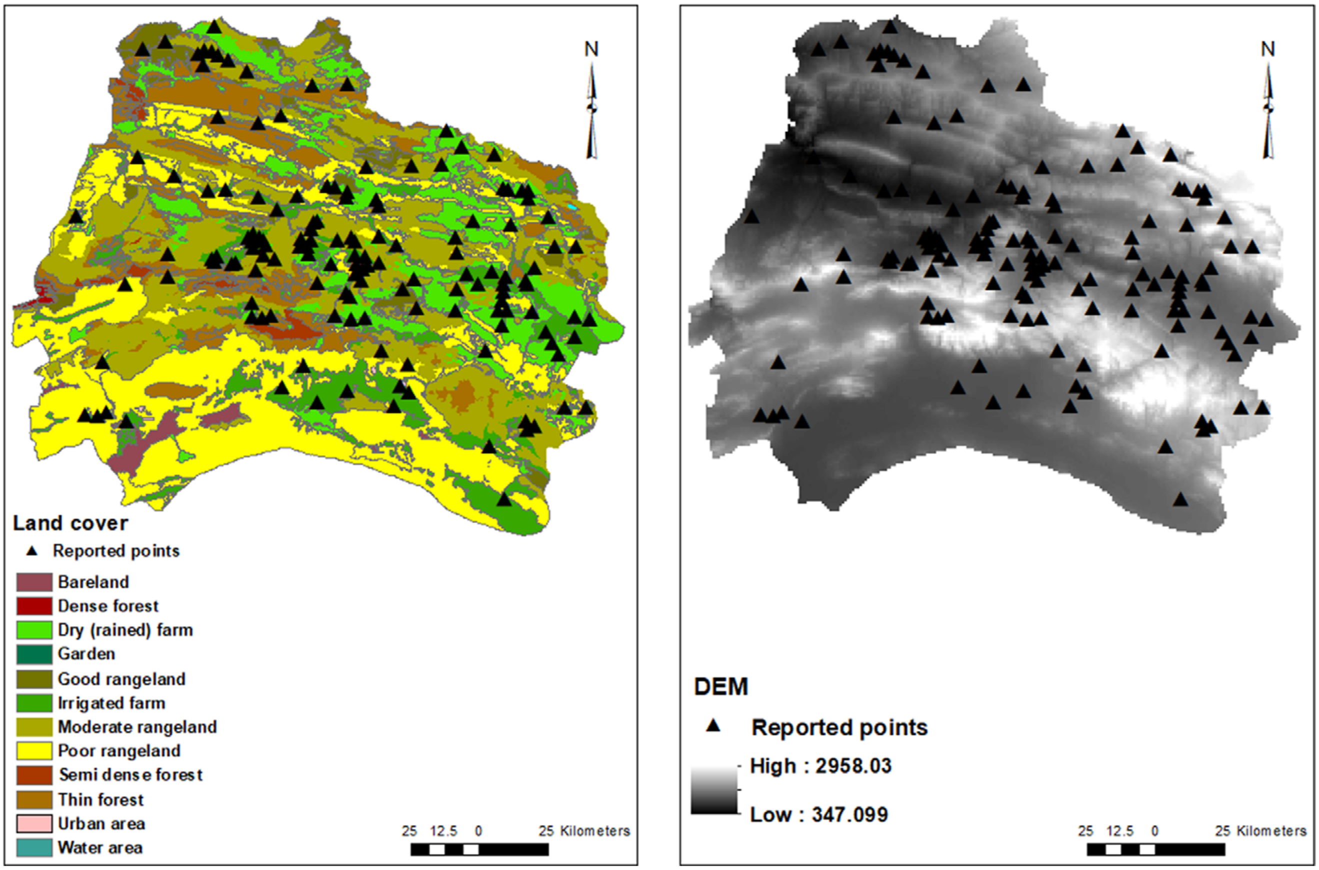

Figure 4. Land covers and digital elevation model (DEM). Points with CE were shown by a triangle symbol. Maps legends were created with ArcMap from ArcGIS 10.5.

Table 4. Multivariate analysis of climatic and geographic factors on the distribution of hydatidosis in North Khorasan province

Factors	P value	OR	CI
MinMAT	0.239	1.206	0.883–1.645
MaxMAT	0.051	1.355	0.999–1.837
MAST	**0.021**	0.646	0.445–0.938
MAR	0.827	1.001	.994–1.008
MAH	**0 .028**	1.121	1.012–1.241
Poor rangeland (constant)	0.000		
Moderate and good rangeland	0.122	2.403	0.791–7.301
Thin and semi dense forest	0.682	0.630	0.069–5.762
Garden	0.096	4.571	0.764–27.357
Dry (rained) farm	0.045	3.139	1.028–9.58
Irrigated farm	0.003	4.610	1.659–12.806
Urban area	**< 0.001**	194.150	48.466–777.743
Bareland	0.999	0.000	0.000

MAT = mean annual temperature; maximum MAT = maximum mean annual temperature; minimum MAT = minimum mean annual temperature; MAST = mean annual soil temperature; MAR = mean annual rainfall; MAH = mean annual humidity.

Discussion

Based on GIS data, our analysis shows that the occurrence of human CE in North Khorasan Province, northeastern Iran, is mainly influenced by the land cover of the urban environment and farms, and soil temperature and humidity as climatic factors. When evaluated independently, gardens, good pastures, rainfall, and air temperatures were other determinants.

Urban areas, including cities and large villages, emerged as the most significant land cover type affecting the distribution of CE. Different factors can cause a higher chance of CE occurrences in urban areas. Echinococcus granulosus senso stricto, especially the G1 genotype, is dominant in North Khorasan, so sheep are the main intermediate host in this area. In North Khorasan, *E. granulosus* infects a notable number of canids (6.6%) (Heidari *et al.* 2019). Large sheep husbandries around cities and large villages and a notable number of infected stray dogs seeking food around these areas can make these large residential areas a risk zone for CE. Moreover, people living in suburban areas with more free-roaming dogs often have lower socioeconomic levels. Some of these individuals immigrate from rural or nomadic areas and tend to raise livestock, which can increase interaction between humans, livestock, and stray dogs. A study in San Carlos de Bariloche, Argentina, showed more Echinococcus granulosus-infected roaming dogs were in the lower socioeconomic levels of the city (Flores *et al.* 2022). Also, some households keep dogs and livestock close, allowing infected dogs to contaminate the surrounding environment with faeces containing eggs that cause a higher prevalence of CE in intermediate hosts and, finally, adult worms in dogs. A study conducted in rural areas of Kazakhstan demonstrated a higher prevalence of infection in dogs that are closely associated with livestock compared to those kept as house pets (Torgerson et al.

2003). Traditional livestock management practices such as home slaughtering or traditional butchers' shops and the disposal of infected organs in open areas, along with feeding shepherd dogs with infected viscera in suburban areas, create opportunities for stray or shepherd dogs to consume contaminated materials, thereby perpetuating the cycle of infection (Eslami and Hosseini 1998; Sánchez Thevenet *et al.* 2019; Varcasia *et al.* 2011). Humans and other intermediate hosts can get infected by eating raw or poorly washed food and vegetables from nearby farms contaminated with *E. granulosus* eggs from infected dogs. Most CE patients in Khorasan Razavi, the neighbouring province of North Khorasan, and with similar social and cultural conditions were from urban areas, and the main risk factors for patients were having domestic dogs and inadequately washed vegetables; 64.4% of patients washed the vegetables with water alone (Khazaei *et al.* 2016).

Farming and agricultural activities were other important factors identified in our models. This may be due to the traditional herding of large flocks of sheep and goats in villages and suburban areas. These herds and their sheepdogs, especially after the growing season and harvesting of crops, are grazing on farmlands. Our observation indicates that the dry and irrigated farmlands and many gardens often lack fencing and are located adjacent to many villages and cities in this province. The mobility of dogs, which have a considerable range of activities, facilitates the spread and prevalence of echinococcosis in farmlands (Zeng *et al.* 2014). This is especially important in farming systems that use irrigation since the humidity from the water can help *E. granulosus* eggs stay in the environment (Barosi and Umhang 2024; Ghatee *et al.* 2020). From a cultural point of view, eating raw, fresh hay in nature during New Year (Nowruz) celebrations (personal communication) may make people in this area even more vulnerable to the Echinococcus parasite.

In North Khorasan Province, researchers identified medium- and high-quality pastures as one of the land cover types influencing the occurrence of CE. In pastures, nomadic herders have historically grazed their animals; stray and shepherd dogs and wild canids roam these areas for activity. A review study in China emphasises the role of stray dogs in pastures in contaminating the sheep flocks grazing there (Yang *et al.* 2012). Although agricultural lands have been one of the leading environmental factors of humans (Ghatee *et al.* 2020) and animals (Jamshidi *et al.* 2020) hydatidosis in southwestern Iran, pastures are not a determining factor in those areas. Based on our calculations, pastures cover most (57%) of the area of North Khorasan. They are, therefore, the primary source of grazing for sheep flocks in this province, which could indicate the role of this land cover in the disease circulation. Also, this province is located at a higher latitude in northeastern Iran and has lower temperatures, which could contribute to the higher survival rate of Echinococcus eggs in pastures.

Climatic factors, such as temperature and humidity, can significantly influence the survival and infectivity of *Echinococcus* eggs (Cadavid Restrepo *et al.* 2016; Veit *et al.* 1995; Wachira *et al.* 1991). In the present survey, soil temperature emerged as the most influential climatic factor affecting the occurrence of CE. Moreover, univariate models also revealed a significant relationship between air temperature and CE occurrence. Accordingly, lower soil and air temperatures were associated with a higher chance of hydatidosis. Similarly, Atkinson *et al.* indicated that higher temperatures correlate with reduced incidence of hydatidosis, especially in the northern hemisphere (Atkinson *et al.* 2012). However, a study conducted in Fars province in southwestern Iran found no relationship between air temperature and the occurrence of CE, which was explained by the higher effect of other mentioned factors and the more important role of humidity in the survival of eggs in this mostly semi-arid region of Iran (Ghatee et al. 2020). Soil temperature appears to be more important than air temperature, as *Echinococcus* eggs excreted through canid faeces have more direct and prolonged contact with the ground than with the air. Consistent with our findings, in western China, land surface temperature had a stronger negative association with CE occurrence in the multivariate model, while air temperature was significant only in the univariate model (Huang *et al.* 2018). Likewise, a large-scale study covering 370 counties across 10 provinces of China where CE is endemic found a significant negative correlation between land surface temperature and CE occurrence (Wang *et al.* 2024).

Humidity was another important climatic factor influencing CE occurrence in the current study, where higher humidity resulted in a more significant occurrence of CE. The greater longevity of *E. granulosus* ova with increased humidity has already been shown. We found a survival rate of 50%, 20%, and 5% at 80%, 60%, and 25% relative humidity, respectively (Laws 1968). In the eastern area of Australia, the chance of finding dogs infected with E. granolusus increased with greater values of maximum relative humidity (Harriott *et al.* 2019). Other studies in Iran and China also have shown the effect of higher humidity on the occurrence of CE (Ghatee *et al.* 2020; Yin *et al.* 2022). Higher humidity helps eggs survive in different environmental conditions, so there is a higher chance of intermediate host infection, and overall, humidity appears to be more critical to Taeniid egg survival than temperature (Barosi and Umhang 2024).

Precipitation was another climatic factor influencing the CE occurrence based on the univariate analysis. The prevalence of CE can significantly correlate positively with annual mean precipitation in China (Huang *et al.* 2018), Chile (Colombe *et al.* 2017), and Iran (Jamshidi *et al.* 2020).

Also, a study in France showed chilly and humid areas with higher precipitation were the risk zone of alveolar echinococcosis (AE) (Piarroux *et al.* 2015). Higher precipitation can increase soil moisture. Increased soil moisture, especially in the cool months, greatly enhances the chances of egg survival and subsequently affects persistence in the environment and transmission to intermediate hosts and humans.

Altitude was not a significant factor in the occurrence of CE in North Khorasan, as was the case in a study of human CE in southwestern Iran (Ghatee *et al.* 2020). In contrast, another study of animal CE in a large area in southwestern Iran showed a significant effect of altitude, with higher altitudes increasing the likelihood of animal CE (Jamshidi *et al.* 2020). This may be due to human and animal life differences, including altitude distribution. On the other hand, there are significant differences in the design of these studies. The human CE studies were done in urban and rural areas (points), which was more accurate than the animal CE study at the county level (large polygons). This may explain why the effects of altitude were different in these two types of study designs. Although the two studies in China were both conducted at the county level on human CE, altitude was a significant factor in only one study (Huang *et al.* 2018; Yin *et al.* 2022). It could, therefore, be related to the influence of other factors and the type of geography of the region.

This study had limitations, including the potential discrepancy between the infection site and the patient's residence due to travel and relocation, which could impact accuracy. However, given the sample size, this is unlikely to affect the findings significantly. Additionally, some patients may not exhibit significant symptoms and have yet to visit health centres.

Conclusion

Environmental and climatic factors influence the incidence of CE in North Khorasan. Urban environments, surrounding farms, gardens, pastures, and areas with higher humidity, rainfall, and lower temperatures are risk areas for CE in northeastern Iran. This can generally be related to higher contact of intermediate hosts, including humans, with dogs and the more remarkable survival of *E. granulosus* eggs in these conditions. However, to know more details about the determinants of CE, there is a need for research that integrates GIS, molecular studies, and human behaviour. Current results and a deeper understanding of the interactions among humans, dogs, and intermediate hosts and climatic factors will aid CE control programs and more effective mitigation strategies for hydatidosis in this hyper-endemic region of Iran.

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Author contribution. All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Reza Shafiei, Mohammad Amin Ghatee, Ahmad Gholami, Mahdi Farsi Farmad, Mohammad Pakdaman, Hamid Reza Shoraka, and Kourosh Arzamani. The first draft of the manuscript was written by Reza Shafee, Mohammad Amin Ghatee, Zahra Kanannejad and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability statement. The datasets generated by the survey research during and/or analysed during the current study are available at the time of journal requisition from Dr. Reza Shafiei after getting permission from Vice Chancellor for Research at the North Khorasan University of Medical Sciences.

Consent to participate. Not applicable.

Consent to publication. Not applicable.

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