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ORIGINAL ARTICLE

The Relation between Toxocariasis and Toxoplasmosis co-infection and the presence of Rheumatoid Factor (RF) in people with hydatidosis in Southwestern Iran, from 2013 to 2018

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Abstract Toxoplasmosis, toxocariasis, and hydatidosis are parasite diseases with a very human-like pathway of infection. worldwide including Iran, there are infected people with these infections. Between 2013 and 2018, serum samples were collected from 124 patients with hydatidosis and 124 serums from hydatidiosis free. Samples were examined for the presence of toxocariasis by detecting IgG antibodies, using the ELISA (Enzyme-Linked Immunosorbent Assay) IBL kit and for the presence of IgG antibodies for toxoplasmosis, using the ELISA test. Risk factors such as contact with animal pets; cats and dogs, rural or urban living, age, sex, and Presence of rheumatoid factor (RF) in serum were investigated during the study. The presence of RF was examined using an agglutination test in all confirmed cases of hydatidosis, toxocariasis, and toxoplasmosis. Of the 124 positive cases of hydatidosis, 30 (24.2%), 51 (41.1%) and 15 (12.09%) had toxoplasmosis, toxocariasis and simultaneous infection (toxoplasmosis and toxocariasis), respectively. In people with toxocariasis, rheumatoid factor was reported more frequently than in other cases. The relationship between the prevalence of rheumatoid factor in serum in people with toxocariasis was significant (41.18%). Interaction with dogs and cats and area of residence were identified as risk factors for toxocariasis (P value > 0.005). Although hydatidosis and toxocariasis are Less common infections compare with toxoplasmosis, they are considered a threat to public health in some parts of the world, including Iran. Some factors, such as habitat and interaction with animal pets (dogs and cats), play a more significant role in toxocariasis compared to toxoplasmosis in people with hydatidosis.

Keywords Hydatidosis · Toxocariasis · Toxocariasis · Rheumatoid factor · Iran

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Introduction

Hydatidosis is usually a occupational disease (usually livestock and butchers) caused by Echinococcus granulosus (mainly strain G1) in humans (by ingestion egg excreted in dog faeces) (Budke et al. 2013; Moro and Schantz 2009). In general prevalence of hydatidiosis in men in higher than in women, but this is not related to the gender of the people (the type of traditions and occupations in the infection is effective). The maximum age of infected people with Hydatidosis between 25 and 35 years and the estimated infection of about 1 million people worldwide (Gholami et al. 2018; Harandi et al. 2011). Hydatidosis is usually seen in cysts in the liver, but can also be seen in the lungs, spleen, muscle, bone, and brain (Harandi et al. 2012). Toxocariasis, hydatidosis and toxoplasmosis may have similar symptoms and signs (such as fever, sweating, neurological symptoms, hepatomegaly, etc.) in people (Raissi et al. 2018). Most people with toxocariasis are young children who are used to eating dirty soils(eggs excreted in dogs), but adults also develop parasites (Shields 1984, Holland 2003). The prevalence of toxocariasis among humans ranges from 1.8 to 78% worldwide (Jones et al. 2008). Toxoplasmosis is a very dangerous protozoan infection for pregnant mothers, infants and people with immune deficiency. The prevalence of infection increases with age (Mirzaalizadeh et al. 2018). In terms of infection prevalence, most parasites are more prevalent and the route of transmission to humans is mainly feces of infected cats or eating sheep's meat (although there are other routes of transmission, such as transfusion, organ transplantation, etc.)(Robert-Gangneux and Dardé 2012). In immunocompetent hosts, it is usually asymptomatic or self- limiting, but causes severe disease in immunocompromised and congenital infections, which can lead to ocular disease, microcephaly, and hydrocephaly in the fetus (Furtado et al. 2011; Barbosa et al. 2012). Rheumatoid arthritis(RA) is a common autoimmune inflammatory disturbance with unknown etiology(Firestein 2003, Prasad and Vassiliou 2015). The global prevalence of RA ranges from 0.5–1%(Prasad and Vassiliou 2015). In recent studies, hydatidosis infections increase the risk of RA. Scientists today believe that this parasite infection can increase the risk of developing a variety of diseases, such as rheumatoid arthritis(Hosseininejad et al. 2018). Therefore, the presence of RA in people with confirmed hydatidosis, toxocariasis, toxoplasmosis, and their co-infection was tested in this study. The aim of this study was to determine the seroprevalence of co-infection in hydatidosis, toxocariasis, toxoplasmosis, and the presence of Rheumatoid Factor (RF), and also to identify the role of variable factors such as contact with dogs and cats, age, sex, location, Hydatid cyst location and presence of Rheumatoid Factor associated with these infections in Ahvaz, Southwest of Iran.

Materials and methods

This study was a cross-sectional study conducted between 2013 and 2018 on 124 hydatidosis patients and 124 clinically healthy individuals. Due to the indolent nature of hydatidosis, the present study requires sampling over several years. In addition, serum samples of people with hydatidosis were tested using the antigen B approved by the medical diagnostic laboratory using serologic tests (ELISA). After evaluation of hydatidosis infection, 5 ml of venous blood samples were collected from each participant. All blood samples were left to clot for 24 h at room temperature (RT), then centrifuged for 10 min at 2000 RPM. The serum was then collected in tubes and stored in a freezer at − 70° C in the Parasitology Laboratory for subsequent use.Serum samples were collected for anti- T gondii IgG antibodies using an ELISA) EUROIMMUN kit, and Toxocara IgG antibodies were detected using an ELISA (IBL International GmbH, Hamburg, Germany) kit. All hydatidosis samples were tested for Rheumatoid Factor (IgG) with an rapid latex agglutination test (Omega kit, UK).). Prepare serial dilutions of patients ' serum using isotonic saline (1/2, 1/4, 1/8, 1/16, 1/32, 1/64 and 1/128). Positive results will be obtained at a RF serum concentration of 8 IU/ml or more and negative results will be obtained at a RF concentration below 8 IU/ml (1/titre × 8 = IU/ml). The SPSS software version 20.0 was used for statistical analysis. The Chi square test was used to compare the infection rate.

Findings

Table 1 showed the relationship between different factors (age, sex, place of residence, the presence of serum rheumatoid factor, types of cysts in patients with hydatidosis and association with dogs and cats) and the prevalence of toxoplasmosis in 124 patients with hydatidosis. About one quarter (24.2%) of the individual had IgG anti-toxoplasmosis in their serum. Furthermore, the average age of positive toxoplasmosis cases was 47.4 years. There was no statistically significant relationship between the prevalence of hydatidosis and toxoplasmosis with regard to the presence of Rheumatoid Factor (RF), Contact with dog and cat, Hydatid cyst location and other items (sex, age, location) (P value > 0.005).

Table 2 showed the relationship between different factors (age, sex, place of residence, the presence of serum rheumatoid factor, types of cysts in patients with hydatidosis and contact with dogs and cats) and the prevalence of toxocariasis in 124 patients with hydatidosis. About (41%) of the individual had IgG anti- toxocariasis in their serum. In addition, the average age of positive cases of

Table 1 Prevalence of toxoplasmosis infection in people with hydatidosis

Individuals with hydatidosis	Samples N (%)	Positivity N (%)	Prevalence ratio	*P* value
Variable (Age)				0.570
5–24	18 (14.5)	04 (13.34)	1	
25–44	44 (35.5)	09 (30)	0.7	
45–64	41 (33)	11 (36.66)	0.5	
65 or more	21 (17)	06 (20)	1.15	
Total	124 (100)	30 (100)		
Variable (Sex)				0.063
Male	55 (44.35)	19 (63.34)	1	
Female	69 (55.65)	11 (36.66)	0.46	
Variable (Hydatid cyst location)				0.410
Liver	92 (74.2)	20 (66.66)	1	
Lung	20 (16.1)	06 (20)	0.9	
Others (Kidney, spleen, bone, brain and pancreas)	12 (9.7)	04 (13.34)	1	
Variable (Rheumatoid Factor)				0.236
Negative	92 (74.19)	19 (63.33)	1	
Positive	32 (25.81)	11 (36.67)	1.46	
Variable (Contact with dog and cat)				0.755
Yes	110 (88.7)	26 (86.66)	1	
No	14 (11.3)	04 (13.34)	1. 2	
Variable (Location)				0.785
Urban area	19 (15.3)	04 (13.34)	1	
Rural area			1.18	

Table 2 Prevalence of toxocariasis infection in people with hydatidosis

Individuals with hydatidosis	Samples N (%)	Positivity N (%)	Prevalence ratio	*P* value
Variable (Age)				0.407
5–24	18 (14.5)	11 (21.57)	1	
25–44	44 (35.5)	17 (33.33)	0.5	
45–64	41 (33)	15 (29.4)	0.7	
65 or more	21 (17)	08 (15.7)	0.85	
Total	124 (100)	51 (100)		
Variable (Sex)				0.205
Male	55 (44.35)	28 (54.9)	1	
Female	69 (55.65)	23 (45.1)	0.7	
Variable (Hydatid cyst location)				0.871
Liver	92 (74.2)	37 (72.55)	1	
Lung	20 (16.1)	09 (17.65)	1.02	
Others (Kidney, spleen, bone, brain and pancreas)	12 (9.7)	05 (9.8)	0.97	
Variable (Rheumatoid Factor)				0.045
Negative	92 (74.19)	30 (58.82)	1	
Positive	32 (25.81)	21 (41.18)	2.01	
Variable (Contact with dog and cat)				0.046
Yes	110 (88.7)	50 (98.04)	1	
No	14 (11.3)	01 (1.96)	0.16	
Variable (Location)				0.035
Urban area	19 (15.3)	02 (3.92)	1	
Rural area	105 (84.7)	49 (96.08)	4.43	

toxocariasis was 42.6 years. There was no statistically significant relationship between the prevalence of hydatidosis and toxocariasis in relation to Hydatid cyst location (P value > 0.005). However, there was a significant correlation between environmental factors (association with dogs and cats) and rheumatoid factor in serum with (96.07%) people with toxocariasis living in rural areas and (98.04%) in close contact with dogs and cats. Also, (41.20%) people with hydatidosis who had positive anti-toxocariasis IgG had a rheumatoid factor in their own serum ($P < 0.005$).

A total of 124 cases of hydatidosis aged 5–75 years participated in this study. The modal age for hydatidosis cases was 25–44 (33.34%). The average age of positive toxocariasis and toxoplasmosis cases, however, was 43.9 years. About (12.9%) of cases of hydatidosis were simultaneously infected with toxoplasmosis and toxocariasis, but there was no significant relationship between co-infection with toxocariasis and toxoplasmosis with regard to the presence of Rheumatoid Factor (RF), Contact with dog and cat, Hydatid cyst location and other items in people with hydatidosis (P value > 0.005).

Table 4 shows that the prevalence of toxocariasis and co-infection among people with hydatidosis is much higher than among Hydatidosis free. However, the prevalence of toxoplasmosis in Hydatidosis free is slightly higher than hydatidosis (P value > 0.005).

Figure 1 shows the prevalence of toxocariasis, toxoplasmosis and co-infection among people with hydatidosis and Hydatidosis free. Figure 2 also shows the seroprevalence of rheumatoid factor only in hydatidosis and hydatidosis individuals with various contaminations (toxocariasis, toxoplasmosis, and co-infection).

Discussion

This seroprevalence study showed that the prevalence of toxocariasis and toxoplasmosis in hydatidosis patients varies widely with sex and other factors such as the

Table 3 Prevalence of toxoplasmosis and toxocariasis coinfection in individuals with hydatidosis

Individuals with Hydatidosis	Samples N (%)	Positivity N (%)	Prevalence ratio	*P* value
Variable (Age)				0.825
5–24	18 (14.5)	03 (20)	1	
25–44	44 (35.5)	05 (33.34)	0.85	
45–64	41 (33)	04 (26.66)	0.7	
65 or more	21 (17)	03 (20)	1.2	
Total	124 (100)	15 (100)		
Variable (Sex)				0.253
Male	55 (44.35)	09 (60)	1	
Female	69 (55.65)	06 (40)	0.54	
Variable (Hydatid cyst location)				0.903
Liver	92 (74.2)	11 (73.34)	1	
Lung	20 (16.1)	03 (20)	1.26	
Others (Kidney, spleen, bone, brain and pancreas)	12 (9.7)	01 (6.66)	0.66	
Variable (Rheumatoid factor)				0.246
Negative	92 (74.19)	09 (60)	1	
Positive	32 (25.81)	06 (40)	1.92	
Variable (Contact with dog and cat)				0.873
Yes	110 (88.7)	14 (93.34)	1	
No	14 (11.3)	01 (6.66)	0.51	
Variable (Location)				0.640
Urban area	19 (15.3)	03 (20)	1	
Rural area	105 (84.7)	12 (80)	0.7	

environment and contact with animal pets in Khuzestan province, Western Iran. Many researchers have reported the prevalence of hydatidosis among different populations (Dabaghzadeh et al. 2018, Han et al. 2018; Dabaghzadeh et al. 2018; Vaidya et al. 2018). Nevertheless, the living environment and history of contact with cats and dogs in the population have influenced the prevalence of co-infection with other parasite diseases(Beiromvand et al. 2018). We found that one of the most important factors contributing to hydatidosis infection with toxocariasis and toxoplasmosis was the association of individuals with dogs and cats, mainly due to the conditions of the surrounding environment. In addition, the presence of rheumatoid factor in patients was associated with toxocariasis co-infection.A study reported by Jones et al. (2008)showed a significant risk of co-infection between toxoplasmosis and toxocariasis among Americans. The results showed the seroprevalence of toxoplasmosis and toxocariasis of 23.6% and 14.0% respectively, and the risk factors showed that people infected with toxocariasis are more likely to be infected with toxoplasmosis and, likewise, people infected with toxoplasmosis are more likely to be infected with toxocariasis(Jones et al. 2008). In the present study, we found that the prevalence of hydatidosis co-infection with toxoplasmosis and toxocariasis was 12.1%. The role of environmental factors in patients with hydatidosis and toxocariasis was noted. There was also a high prevalence of rheumatoid factor in patients with positive anti- toxocariasis antibodies (41.18%). Compared to healthy controls, contact with dogs and cats and living in rural areas appears to have increased the risk of co-infection among infected individuals. A study conducted in Turkey by Alım et al. (2017) reported that patients with Echinococcus infection developed right- knee arthritis. Due to increased inflammatory factors (such as RF), hydatidosis patients are considered for skeletal disorders. Another study in 2016 reported that a 3-year- old girl had co-infection with toxocariasis and chronic arthritis. It is important that zoonotic parasite diseases are considered in patients with arthritis(Viola et al. 2016). A meta-analysis study on seroprevalence of toxoplasmosis in rheumatoid arthritis patients reported that of 1396 patients with rheumatoid arthritis, 46% had a positive toxoplasmosis infection. It can be concluded that toxoplasmosis could be a potential risk factor for RA(Hosseininejad et al. 2018). Although the serum level of rheumatoid factor was found to have increased in people with toxoplasmosis in the previous study, we observed an increase in rheumatoid factor in patients with hydatidosis who had anti- toxocariasis antibodies (41.18%). According to some geoepidemiological studies, host susceptibility, lifestyle, environmental factors, dietary and environmental pollution can increase the risk of developing autoimmune diseases(Shapira et al. 2012). A study on the prevalence of hydatidosis and toxocariasis among rural people in southwestern Iran reported that 4.9% were positive for hydatidosis, and 2% were positive for toxocariasis. There was a significant difference between occupational types and seropositivity, but no significant difference was observed between age, gender and

Table 4 Comparison infection in people with Hydatidosis and Hydatidosis free

Prevalence (%)	Toxoplasmosis (%)	Toxocariasis (%)	Co infection	*P*-Value
People with hydatidosis	24.19	41.12	12.1	0.000
Hydatidosis free	28.22	7.25	2.42	

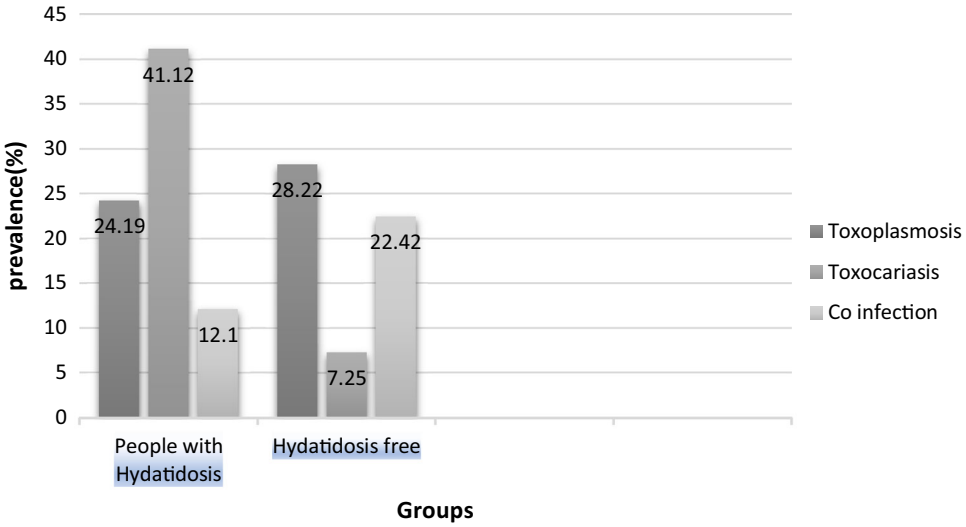

Fig. 1 Comparison Prevalence of infection in people with Hydatidosis and Hydatidiosis free

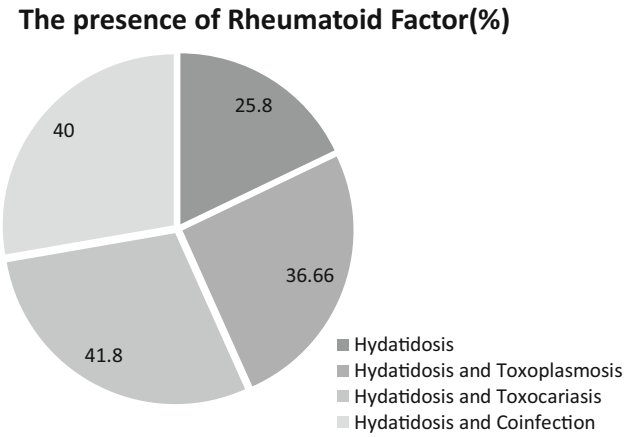

Fig. 2 The presence of rheumatoid factor in people with hydatidosis Based on the type of infection

education levels(Beiromvand et al. 2018). In various studies conducted by researchers, there is a significant relationship between climate change (seasonal variation and rainfall) and an increased prevalence of hydatidosis in humans due to increased chances of survival of parasite eggs in the environment, changing behavior of life People are associated with animals (increasing livestock breeding and more people connecting with dogs).(Cadavid et al. 2018; McMahon; Thevenet et al. 2019). In this study, close contact with animal pets (dogs and cats) was significantly associated with toxocariasis- hydatidosis co-infection and a statistically significant difference were also observed between hydatidosis and toxocariasis infections compared to Hydatidosis free. In addition to exposure to contaminated soil, living in rural areas, sex and age increase the likelihood of exposure to hydatidosis, toxocariasis, and toxoplasmosis as ingestion of undercooked or raw meat (Jones et al. 2008; Ma et al. 2018). The risks to hydatidosis, toxocariasis and toxoplasmosis and their co-infection have been reported to be significantly high in Northern and Southern Iran(Sadjjadi 2006; Ilbeigi et al. 2015). In another study, the prevalence of hydatidosis was up to 64% in domestic animals and this played a key role in transmitting co-infection of hydatidosis and toxocariasis to humans(Eslami and Hosseini 1998; Zhang et al. 2015). The two previous studies, like the present study, showed that co-infection with hydatidosis and toxocariasis is more likely to be due to the similarity in their route of transmission (human contact with infected dogs) and the type of residence.

Conclusion

Although hydatidosis and toxocariasis are considered neglected infections, they are considered a threat to public health in some parts of the world, including Iran. On the other hand, this study showed that environmental factors, such as habitat and close interaction with animal pets (dogs and cats), play a more significant role in toxocariasis compared to toxoplasmosis in people with hydatidosis. In addition, there is a significant increase in the serum rheumatoid factor in hydatidosis patients co-infected with toxocariasis, which indicates that toxocariasis infection has a negative effect on the health of hydatidosis patients.

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Author's contribution Study concept and design: MFK, VR, AR, acquisition of data: OR, MG, EA, ZM, PJ, MS, analysis and interpretation: VR, ZM, SKA, MFK.

Compliance with ethical standards

Conflict of interest The authors and coauthors declare that they have no conflict of interest that affects this study.

Ethical statement Health Research Institute Ethical Board of Infectious and Tropical Diseases Research Centre, Ahvaz Jundishapur University of Medical Sciences, Iran approved. Prior to collecting blood samples.

Informed consent Informed consent was obtained from all participants included in the study.

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