Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2016, 5, 11:204-208

No Evidence of Association between *Toxocara canis* Infection and Cancer Risk

Seyyed Mohammad Mousavi[1], Ahmad Hosseini-Safa[1], Hossein Mahmoudvand[2], Mehran Bagh Bahadorani[1], Shayan Mostafaei[3] and Hossein Yousofi Darani[4]*

[1]*Department of Medical Parasitology and Mycology, Isfahan University of Medical Sciences, Isfahan, Iran*
[2]*Hepatitis Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran*
[3]*Division of Biostatistics, Department of Epidemiology and Biostatistics, School of public Health, Isfahan University of Medical Sciences, Isfahan, Iran*
[4]*Infectious and Tropical Disease Research Center, Isfahan University of Medical Sciences, Isfahan, Iran*
**Corresponding E-mail: H_yousofi@yahoo.com*

ABSTRACT

Nowadays, it has been proven that infection with some pathogens, such as certain viruses, bacteria, and parasites, is one of the most important and preventable causes of cancer worldwide. Human toxocariasis is a helminthic zoonosis infection caused by the larvae of the ascarid worms of Toxocara spp. The present study aims to evaluate the seroprevalence anti-T. canis antibodies among cancer patients from Isfahan province, Central, Iran. A total of 97 patients including 16 prostate, 48 gastrointestinal tracks (GIT), and 33 breast cancer patients referred to the Seyedo-Shohada hospital in Isfahan city, central Iran and 30 healthy volunteers as control group were screened for IgG anti-T. canis antibody by enzyme linked immunosorbent assay (ELISA). Structured questionnaires were used to obtain information on risk factors for T. canis infection. Totally, 3 (2.4%) samples from both groups were found seropositive for anti-T. canis antibodies. None of the 16 prostate cancer patients were positive for anti-Toxocara antibody; whereas 4.2% (2/48) and 3.1% (1/33) of GIT and breast cancer patients were found positive for anti-T. canis antibodies, respectively. There was no significant difference in T. canis IgG positivity between the cancer patients and control group (p= 0.2). The results showed contact with dog was not associated with the seropositivity of T. canis. According to the obtained results, there was no evidence of association between T. canis infection and cancer risk. However, further studies should explore T. canis-related effects on cancer risk in larger sample size.

Key words: Toxocariasis, Cancer, ELISA, IgG

INTRODUCTION

Human toxocariasis is a helminthic zoonosis infection caused by the larvae of the ascarid worms of *Toxocara* spp. Dog roundworms, *Toxocara canis*, and cat roundworms, *T. cati* are recognized as causative agents of human toxocariasis which the small intestines of definitive hosts [1]. Humans as accidental host can be infected by ingestion of soil, water, or food contaminated with embryonated ova; whereas consumption of chicken and cow livers is another rare route [2]. The majority of human toxocariasis among immunocompetent people is usually asymptomatic; however severe diseases and complications can occur due to organ injury by migrating larvae [1,3]Clinical symptoms of toxocariasis are classified as visceral larva migrants (VLM), ocular larva migrants (OLM), neurologic, and covert toxocariasis [1].

Cancer is a one of the main cause of death worldwide, accounting for approximately 7.6 million deaths (13% of all deaths) [4]. It is predicted that deaths from cancer are projected to continue to rise, with an estimated 11 million deaths in 2030 [5]. At present, nearly one third of cancer cases could be decreased if diagnosis and treatment have been carried out at an early stage [6]. Nowadays, it has been proven that infection with some pathogens, such as certain viruses, bacteria, and parasites, is one of the most important and preventable causes of cancer worldwide; so that approximately a fifth of cancers are incurred by infectious agents in the world [7-9].

Cancers caused by infections generally have a higher mortality rate than other one [4].Several studies have reported an adverse relationship between some parasite infections and cancer in the human population worldwide [10]. To best of our knowledge, there is no study on association between human toxocariasis and cancer in Iran. Therefore, the present study aims to evaluate the seroprevalence anti-*T. canis* antibodies among cancer patients from Isfahan province, Central, Iran.

MATERIALS AND METHODS

Ethics
This study was approved by Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran. In addition, a written informed consent was obtained from all the participants before blood sampling.

Questionnaire
Before collection of blood samples, the applied questionnaire was based on demographic data including age, gender, and education. Moreover, possible risk factors, such as animal contacts (dog), and residence were also evaluated.

Study design
This case-control study was performed in two populations: patients with three types of cancer (breast, gastrointestinal tract and prostate) confirmed by an oncologist consultant and healthy individuals from May 2013 to May 2014 in the Isfahan province, Iran. Totally, 97 patients including 16 prostate, 48 gastrointestinal track (GIT), and 33 breast cancer patients referred to the Seyedo-Shohada hospital in Isfahan city, central Iran were invited to participate in this study. Furthermore, 30 healthy volunteers were selected as control group.

Sample collection
Five mL of blood was obtained from each of the patient and healthy subjects by means of venipuncture, under sterile conditions. The samples were centrifuged at 1000 r.p.m. and the sera were stored at 20°C until serological examination. All samples were tested blind such that the person performing the assay was not aware of the identity of the samples.

Enzyme-linked immunosorbent assay
To determine the anti-*T. canis* antibodies, serum samples were transported to Parasitology Laboratory, Department of Parasitology and Mycology, Isfahan University of Medical Sciences (Isfahan, Iran) and stored at -20˚C until being tested. All the serum samples were tested using the commercially IBL Germany (anti IgG-*Toxocara*) Kit according to the manufacturer's instructions. The reaction cut-off was calculated as the mean optical density (OD) for negative control sera plus three standard deviations. The positive and negative control sera were included in each plate and were obtained from the kit. The reading was performed using a microplate reader (Bio-Tek, USA) set at a level of absorbance of 450 nm. All samples were run in triplicate. The results were considered positive when OD_{450} index was equal or higher than the cut-off value in ELISA [11].

Statistical analysis
Statistical analysis was carried out using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). Logistic regression models were used to evaluate association between *T. canis* seropositivity and the potential risk factors. $p<0.05$ was considered to be statistically significant.

RESULTS

Participants
A total of 127 samples were included in the present study; including 97 cancer patients (16 prostate, 48 GIT, and 33 breast cancer patients) and 30 healthy volunteers as control group. The mean age of the participants was 51 years old

(ranging from 39 to 71 years old). Most participants were male (55.1%), aged 51-60 years old, living in urban areas (72.4%), who had not college education (less than diploma) (59.8%) (Table 1).

Table 1. Distribution of anti-*Toxocara* antibodies in cancerous patients compared with healthy controls based on age, sex, education level, place of residence and contact with dog.

Risk factors	No. (%) of analyzed samples	No. (%) of posetive	No. (%) of negative	OR	OR(95%Cl)	P value
Cancer						
No cancer	30(23.6)	0(0.0)	30(100)			
Prostate	16(12.6)	0(0.0)	16(100)	-	-	0.611
Gastrointestinal track	48(37.8)	2(4)	46(96)			
Breast	33(26)	1(3)	32(97)			
Sex						
Male	70(55.1)	1(1.4)	69(98.6)	0.399	0.035<OR<4.511	0.442
Female	57(44.9)	2(3.5)	55(96.5)			
Residency						
Rural	35(27.6)	2(5.7)	33(94.3)	0.181	0.016<OR<2.066	0.154
Urban	92(72.4)	1(1.1)	91(98.9)			
Ownership and contact with dogs	33(26)	1(3)	32(97)	1.438	0.126<OR<16.393	0.775
Yes	94(74)	2(2.1)	92(97.9)			
No						
Parents education						
Diploma&Less than	76(59.8)	1(1.3)	75(98.7)	3.061	34.678<OR<0.270	0.349
Higher than diploma	51(40.2)	2(3.9)	49(96.1)			
Disease						
Safe	30(23.6)	0(0.0)	30(100)		-	0.20
Cancer	97(76.4)	3(3.1)	94(96.9)			

Seroprevalence of anti-*T. cati* antibodies

Totally, 3 (2.4%) samples from both groups were found seropositive for anti-*T. canis* antibodies;

Out of the 97 cancer patients, 3 (3.1%) patients tested seropositive for anti-*T. canis* antibodies. None of the 16 prostate cancer patients were positive for anti-*Toxocara* antibody; whereas 4.2% (2/48) and 3.1% (1/33) of GIT and breast cancer patients were found positive for anti-*T. canis* antibodies, respectively. Moreover, none of the 30 healthy volunteers were positive for anti-*Toxocara* antibody. There was no significant difference in *T. canis* IgG positivity between the cancer patients and control group (p= 0.2).

Out of 70 (55.1%) male participants, 1 (1.4%) tested seropositive for anti-*T. canis* antibodies; whereas from 57 (44.9%) female participants, 2 (3.5%) tested seropositive for anti-*T.canis* antibodies. There was no significant difference in the prevalence of anti-*T.canis* antibodies among the female and male patients (p = 0.442). As shown in Table 1, there was no significant difference in the prevalence of anti-*T.canis* antibodies among the in patients living in urban and those living in rural areas (p = 0.154). By aging, comparing the seroprevalence adjusted by age, the differences between cancer patients and healthy participants were not significant in any of the age subgroups (p= 0.673). Out of 33 (26%) participants who contacting with dog, 1 (3%) tested seropositive for anti-*T. canis* antibodies; whereas from 94 (74%) participants who no contacting with dog, 2 (2.1%) tested seropositive for anti-*T. canis* antibodies. There was no significant association with *T. canis* seropositivity in cancer patients who are being in contact with dog (p= 0.774).

DISCUSSION

In the present investigation, for the first time in Iran, we evaluated the seroprevalence of anti-*T. canis* antibodies among cancer patients from Isfahan province, Central, Iran. The obtained findings demonstrated that from 97 cancer patients, 3 (3.1%) samples were seropositive for anti- *T. canis* antibodies; while none of the 30 healthy volunteers were positive for anti-*Toxocara* antibody. Regarding epidemiological situation of toxocariasis in Iran, Abdi et al (2012) have reported that seropositivity for human toxocariasis, soil contamination for *Txocara* spp. eggs and dogs or cats infections with adult worm were 15.8%, 21.6% and 26.8%, respectively [12].Furthermore, in a study conducted by Hoseini Safa et al. (2014) on 427 children whit 5-15 years old referred to the general hospitals of Isfahan province (Central, Iran), 1.39% of the samples had anti-*Toxocara* antibody [11].

Reviews have reported that many infections are established causes of cancer. For example, the virus Human *Papillomavirus* causes virtually all cervical cancers along with several other types, while hepatitis B and C cause liver cancer. The bacterium *Helicobacter pylori* can lead to stomach cancer. Among the parasitic infection, the Termatode of *Schistosoma*, can increase the risk of bladder cancer [13]. In contrast, other studies revealed that parasitic infections can induce resistance to the tumor development. For example, *Trypanosoma cruzi* infection confers resistance to the tumor development in mice, and also in vitro studies have shown toxic effects of parasite extracts on the cancer in cell cultures [14,15,]. In addition, *Toxoplasma gondii* infection inhibits the tumor growth in certain types of cancers in mouse models through induction of Th1 immune responses and antiangiogenic activities [16]. Recently, Yousofi Darani et al (2009) have also reported that *T. gondii* parasites and *T. canis* egg antigens induce inhibition of the tumor growth in the fibrosarcoma mouse model [17].

The obtained findings demonstrated that there was no significant difference in seroprevalence of *T. canis* infection between the cancer patients and control group. Based on the obtained results, we found that there was no significant association in *T. canis* IgG positivity between the male and female individuals in both groups. Similarly in several studies there were no significant differences in *T. canis* IgG positivity between males and females (11, 18, 19).We did not find any statistically significant difference in *T. canis* IgG positivity when age groups were compared. Consistent with our results, various investigations were not found any significant association in *T. canis* IgG positivity when age groups were compared (11, 18, 19). This might be explained by the limited size of the sample in each age group. The obtained findings in the present study revealed there is no statistically significant difference in seroprevalence of anti-*T. canis* IgG antibody between individuals living in urban and rural areas both groups. According to these findings, residential area has no effect on the risk of the toxocariasis. In line with our results Hosseini Safa et al (2015) found that individuals living in urban and rural areas in Iran did not have significant difference in the seroprevalence of *T. canis* infection (11). In contrast to our finding, Sadjjadi et al. demonstrated a significant correlation between places of living with seropositivity of toxocariasis (18). Here, we found that there was no significant there was no significant relationship contact with dog with seroprevalence of anti-*T. canis* IgG antibody. Consistent with our findings, several investigations revealed there is no statistically significant difference between seroprevalence of anti-*T. canis* IgG antibody and contact with dog (11, 20).

CONCLUSION

According to the obtained results, there was no evidence of association between *Toxocara canis* infection and cancer risk. However, further studies should explore *T. canis*-related effects on cancer risk in larger sample size.

Acknowledgment
This work was supported by Isfahan University of Medical Sciences, Grant Number190138.

REFERENCES

[1] Fialho PM, Corrêa CR. A Systematic Review of Toxocariasis: A Neglected but High-Prevalence Disease in Brazil. Am J Trop Med Hyg. 2016;1: 15-0733.
[2] Smith H, Holland C, Taylor M, Magnaval J, Schantz P, Maizels R. How common is human toxocariasis? Towards standardizing our knowledge. Trends in Parasitology. 2009;25(4):182-8.
[3] Heuer L, Haendel S, Beineke A, Strube C Effects of Toxocara larvae on brain cell survival by in vitro model assessment. Parasitology. 2015; 142(10):1326-34.
[4] Cannon G, Gupta P, Gomes F, Kerner J, Parra W, Weiderpass E, et al., Prevention of cancer and non-communicable diseases, Asian Pac. J. Cancer Prev. 2012; 13: 3–11.
[5] WHO –World Health Organization, Cancer, Fact. Sheet 297, 2011.
[6] International Agency for Research on Cancer (IARC), Working Group, Agents Classified by the IARC Monographs, IARC, Lyon (France), 2008.
[7] Ahmed HG, Awareness survey on knowledge of microbial infectious causes of cancer in northern state of Sudan, Asian Pac. J. Cancer Prev. 2012; 13: 5497–5500.
[8] Bouvard V, Baan R, Straif R, Grosse Y, Secretan B, Benbrahim-Tallaa L, et al., WHO international agency for research on cancer monograph working group. a review of human carcinogens – part b: biological agents, Lancet Oncol. 2009; 10: 321–322.
[9] Zur Hausen H. *Streptococcus bovis*: causal or incidental involvement in cancer of the colon?, Int. J. Cancer 2006; 119: 11–12.

[10] Darani HY, Yousefi M. Parasites and cancers: parasite antigens as possible targets for cancer immunotherapy. Future Oncology. 2012;8(12):1529-35.
[11] Hosseini-Safa A, Mousavi SM, Bahadoran Bagh Badorani M, Ghatreh Samani M, Mostafaei S, Yousofi Darani H. Seroepidemiology of Toxocariasis in Children (5-15 yr Old) Referred to the Pediatric Clinic of Imam Hossein Hospital, Isfahan, Iran.Iran J Parasitol. 2015;10(4):632-7.
[12] Abdi J, Darabi M, Sayehmiri K. Epidemiological situation of toxocariasis in Iran: meta-analysis and systematic review. Pak J Biol Sci. 2012; 15(22):1052-5
[13] De Flora S and La Maestra S. Epidemiology of cancers of infectious origin and prevention strategies. J Prev Med Hyg. 2015; 56(1): E15–E20.
[14] Kallinikova VD, Matekin PV, Ogloblina TA, Leikina MI, Kononenko AF, Sokolova NM, Pogodina LS. Anticancer properties of flagellate protozoan *Trypanosoma cruzi* Chagas. Izv Akad Nauk Ser Biol. 2001; 3:299–311.
[15] Atayde VD, Jasiulionis MG, Cortez M, Yoshida N. A recombinant protein based on*Trypanosoma cruzi* surface molecule gp82 induces apoptotic cell death in melanoma cells.Melanoma Res. 2008; 18:172–183.
[16] Kim JO, Jung SS, Kim SY, Kim TY, Shin DW, Lee JH, Lee YH. Inhibition of Lewis lung carcinoma growth by *Toxoplasma gondii* through induction of Th1 immune responses and inhibition of angiogenesis. J Korean Med Sci. 2007; 22(Suppl):S38–S46.
[17] Darani HY, Shirzad H, Mansoori F, Zabardast N, Mahmoodzadeh M. Effects of Toxoplasma gondii and Toxocara canis antigens on WEHI-164 fibrosarcoma growth in a mouse model. The Korean journal of parasitology. 2009;47(2):175-7.
[18] Sadjjadi S, Khosravi M, Mehrabani D, Oryan A. Seroprevalence of *Toxocara* infection in school children in Shiraz, Southern Iran. J Trop Pediatr. 2000; 46(6): 327– 30.
[19] Fan CK, Hung CC, Du WY, Liao CW, Su KE. Seroepidemiology of *Toxocara canis* infection among mountain aboriginal schoolchildren living in contaminated districts in eastern Taiwan. Trop Med Int H/ealth. 2004; 9(12): 1312– 8.
[20] Fallah M, Azimi A, Taherkhani H. Seroprevalence of toxocariasis in children aged 1–9 years in western Islamic Republic of Iran, 2003. East Mediterr Health J. 2007; 13(5): 1073– 7.