



# Prevalence and associated risk factors of *Cystoisospora belli* and *Cyclospora cayetanensis* infection among Iranian patients with colorectal cancer

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**Abstract** From among intestinal parasites, coccidian intestinal parasites such as *Cystoisospora belli* (previously known as *Isospora belli*), and *Cyclospora cayetanensis* are well-known as opportunist parasites, particularly in patients with cancer. This study assessed the prevalence of *C. belli* and *C. cayetanensis* in patients with cancer in Lorestan Province, Southwest of Iran. This cross-sectional descriptive study was conducted on 87 patients with colorectal cancers, referred to the general hospitals of Lorestan from October 2017 to August 2018. A fresh stool specimen was collected from each subject in a sterile labeled container. The collected stool samples were concentrated through sucrose flotation method and then prepared for Ziehl–Neelsen staining for microscopic examination. Demographic and possible risk factors such as age, sex, education, residence, and unwashed vegetable/fruit consumption were collected by an applied questionnaire. Out of the 87 patients with colorectal cancer, eight (9.2%) were found positive for *C. belli* and *C. cayetanensis* infections, with five (5.74%) and three (3.44%) patients positive for *C. belli* and *C. cayetanensis* infections, respectively. Results also showed that sex and unwashed vegetable/fruit consumption were significantly associated

with the prevalence of these parasites ( $p < 0.01$ ). The findings revealed the considerable prevalence of *C. belli* and *C. cayetanensis* in patients with colorectal cancers. It is therefore essential for gastrointestinal specialists to pay special attention to the prevalence of coccidian parasites in patients with colorectal cancer.

**Keywords** Cancer · Coccidian parasite · Ziehl–Neelsen staining · Iran

## Introduction

Nowadays, cancer is one of the main causes of mortality in different communities worldwide (WHO 2015). In recent years, with an increase in cancer risk factors such as dietary changes, stresses, environmental changes, and certain infections, it is anticipated that, by 2030, more than 10 million people in the world will die due to cancer (Bouvard et al. 2009; WHO 2015). In the category of existing cancers, colorectal cancer is one of the most abundant gastrointestinal tract cancers considered as the second and third cause of death in women and men, respectively (De Rosa et al. 2015).

Global studies have reported that approximately 25% of the world's population, especially in developing countries, is infected with intestinal parasites (Alemu et al. 2011). In recent years, in spite of increased awareness of parasitic infections as well as sanitation and hygiene development, these infections are still an important health problem.

It has previously been proven that parasitic infections can result in serious clinical complications in immunocompromised individuals (Marcos and Gotuzzo 2013). Patients with cancer are immunocompromised, either as a result the disease itself or because of therapeutic drugs or

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processes leading to immunosuppression (Silva et al. 2011; Utzinger et al. 2012). Therefore, it is crucial that the prevalence of intestinal parasites be determined in these patients.

From among the intestinal parasites, coccidian intestinal parasites such as *Cryptosporidium* spp., *Cystoisospora belli* (previously known as *Isospora belli*), and *Cyclospora cayetanensis* are well-known as opportunist parasites, particularly in patients with cancer (Vento and Cainelli 2003). Although the prevalence of these intestinal parasites has been investigated in various groups of immunocompromised patients, few studies have focused on the prevalence of these parasites in patients with cancer (Oliveira 2014). Therefore, the present study was designed to assess the prevalence of *C. belli* and *C. cayetanensis* in patients with cancer in Lorestan Province, Southwest Iran.

## Materials and methods

### Study area

Lorestan Province is located in western Iran in the Zagros Mountains. It covers an area of 28,392 km<sup>2</sup> and the population of this province was estimated at 1,716,527 people. The main cities are Khorramabad, Borujerd, Aligudarz, Dorud, Kuhdasht, Azna, Aleshtar, Nurabad, and Pol-e Dokhtar (Mahmoudvand et al. 2018).

### Ethics

This investigation was permitted by Ethics Committee of Lorestan University of Medical Sciences (Khorramabad, Iran) with code No. 2019/2048.

### Informed consent statement

In this study, written informed consent was provided by patients before sample collection.

### Study design

This cross-sectional descriptive study was performed on 87 patients with colorectal cancers, referred to the general hospitals of Lorestan from October 2017 to August 2018. Colorectal cancer was confirmed by a gastroenterologist. In this study, patients who had received systemic antibiotics in recent weeks and those with immune deficiencies such as AIDS were excluded.

## Questionnaire

Some demographic and risk factors, including age, sex, education level, residence, and unwashed vegetable/fruit consumption were obtained through a questionnaire.

## Sample collection and processing

From each patient, a stool sample was taken in a sterile labeled container. After obtaining the samples, they were transferred to the Laboratory of Parasitology, School of Allied Medicine (Khorramabad, Iran) (Mahmoudvand et al. 2018), and were then concentrated by the sucrose flotation technique (Sheather's method). In the next step, each sample was smeared on glass slides, air-dried, fixed with methanol, and stained by modified Ziehl–Neelsen. Finally, stained smears were assessed under a light microscope with powers  $\times 10$ ,  $\times 40$  and  $\times 100$  objectives, respectively, to find the oocysts of *C. belli* and *C. cayetanensis* (Garcia 2001).

## Statistical analysis

SPSS 24.0 software was used for data analysis. Univariate logistic regression was also applied to find the correlation between the prevalence of parasites and associated risk factors, and the level of significance was set at  $p < 0.05$ .

## Results

### Participants

A total of 87 patients with colorectal cancer referred to the general hospitals of Lorestan were investigated to assess the prevalence of *C. belli* and *C. cayetanensis*. The mean age of the participants was  $59.6 \pm 6.8$  years, with minimum and maximum values of 36 and 86 years, respectively. The majority of participants were male (51, 58.2%), and most participants lived in urban regions (58, 66.7%).

From among the participants, 80 (92%), 52 (59.8%), and 33 (37.9%) performed hand washing before eating and agricultural activity, and consumed unwashed fruits and vegetables, respectively (Tables 1 and 2).

### Prevalence of *C. belli* and *C. cayetanensis* infections

Out of 87 patients with colorectal cancer, 8 (9.2%) were found positive for *C. belli* and *C. cayetanensis* infections, and 5 (5.7%) and 3 (3.5%) patients were positive for *C. belli* and *C. cayetanensis* infections, respectively (Table 3).

In terms of sex, 6 (11.8%) men and two (5.5%) women were found positive for parasitic infections. There was a

**Table 1** Demographic characteristics and prevalence of *C. belli* and *C. cayetanensis* infection among the participants

Variables	No. (%)	No. (%) of positives	P value
Gender			
Male	51 (58.2)	6 (11.8)	0.01*
Female	36 (41.8)	2 (5.5)	
Age group			
< 30 yrs	11 (12.6)	1 (9.1)	
30-45 yrs<	32 (36.8)	3 (9.4)	
45 yrs<	44 (50.6)	4 (9.1)	
Residence			
Rural	29 (33.3)	3 (10.3)	
Urban	58 (66.7)	5 (8.6)	

\*Was significantly different

**Table 2** Association between risk factors and prevalence of *C. belli* and *C. cayetanensis* infection among the participants

Variables	No. (%)	No. (%) of positives	P value
Hand washing			
Yes	80 (90.2)	7 (8.7)	–
No	10 (9.8)	1 (10)	
Consumption of unwashed fruit/vegetables			
Yes	33 (37.9)	7 (21.2)	0.001*
No	54 (62.1)	1 (1.85)	
Agriculture activity			
Yes	52 (59.8)	5 (9.6)	–
No	35 (40.2)	3 (8.5)	

\*Was significantly different

**Table 3** Prevalence of *C. belli* and *C. cayetanensis* infections among the patients with colorectal cancer

Parasite	Positive case no. (%)	Negative cases no. (%)	Total
<i>Cystoisospora belli</i>	5 (5.7)	82 (94.3)	87 (100)
<i>Cyclospora cayetanensis</i>	3 (3.5)	84 (96.5)	87 (100)
Total	8 (9.2)	80 (90.8)	87 (100)

significant association between sex and positivity of these intestinal parasites.

Considering the age groups, the majority of patients belonged to the age group of > 45 years, but there was no significant association between age groups and the prevalence of intestinal parasites.

In terms of residence, from among the patients living in urban areas, parasitic infections were found in five (8.6%), whereas from among the patients residing in rural areas, three (10.3%) were positive for parasitic infections.

From among patients who performed hand washing before eating, *C. belli* and *C. cayetanensis* infections were found in seven (8.7%), while the rate infection was 10% from among patients who performed no hand washing before eating. No significant association was found between hand washing before eating and positivity to these intestinal parasites.

Of the patients who consumed unwashed fruits and vegetables, *C. belli* and *C. cayetanensis* infections were found in seven (21.2%), while only one (1.96%) patient was found positive. There was a significant association between the consumption of unwashed fruits and vegetables and positivity to these intestinal parasites ( $p < 0.001$ ).

Considering agricultural activities, of the 52 patients having agricultural activities, five (9.6%) were positive for intestinal parasitic infections, whereas three (8.5%) patients had no agricultural activity. There was no significant association between agricultural activity and positivity to these intestinal parasites (Tables 1 and 2).

## Discussion

Based on the reports of the National Cancer Institute, nearly 8 million new cases of cancer are reported annually around the world (INCA 2016). From among cancers, colorectal cancer is one of the most frequent gastrointestinal tract cancers, serving as the second and third cause of mortality in women and men, respectively (De Rosa et al. 2015). It has been proven that patients with cancer are susceptible to opportunistic parasitic infections because anticancer agents make them immunocompromised. Thus, these infections may show severe clinical manifestations and even prove to be lethal for these patients (Silva et al. 2011; Vento and Cainelli 2003).

*Cystoisospora belli*, formerly called *I. belli*, is a protozoan parasite residing in the small intestine. Cystoisosporiasis is commonly asymptomatic or has mild digestive symptoms in immunocompetent people, but severe or fatal complications are reported in patients with immune deficiency (Legua and Seas 2013). Another coccidian parasite found in the small intestine is *C. cayetanensis*. Cyclosporiasis causes persistent diarrhea, and certain clinical manifestations such as abdominal pain, nausea, vomiting, fatigue, fever, and loss of appetite are related to this infection (Herwaldt 2000).

The present study was designed to assess the prevalence of *C. belli* and *C. cayetanensis* in patients with cancer in Lorestan. Out of 87 patients with colorectal cancer, eight (9.2%) were found positive for *C. belli* and *C. cayetanensis* infections, and five (5.74%) and three (3.44%) patients were positive for *C. belli* and *C. cayetanensis* infections, respectively. Previously, Jeske et al. (2018) demonstrated

that *C. belli* was found in 4.4% of patients with cancer in Southern Brazil.

Guarner et al. (1997) also reported that coccidian parasites such as *Cryptosporidium* and *Isospora* were found in 3% in adult patients with cancer in Mexico. Moreover, Rudrapatna et al. (1997) demonstrated that, from among 1029 patients with cancer in India, *I. belli* was found in 0.1% (16). This difference between our results and those of previous studies may be due to factors such as sample size, geographical conditions, and research method.

Based on the statistical analysis, although there was no significant association between the prevalence of *C. belli* and *C. cayetanensis* and some factors, including age, residence, agriculture activity, and hand washing before eating, a significant correlation was observed between positivity to *C. belli* and *C. cayetanensis* and sex as well as consumption of unwashed fruits and vegetables.

## Conclusion

The findings revealed the considerable prevalence of *C. belli* and *C. cayetanensis* in patients with colorectal cancers. In addition, sex and the consumption of unwashed fruits and vegetables were found to be the related risk factors of infection. It is, therefore, essential for gastrointestinal specialists to pay special attention to the prevalence of coccidian parasites in patients with colorectal cancer.

**Author contributions** HM: Study design-data collection. AS: data collection-microscopic examination. MK: data collection-critical review. ARM: supervisor-writing.

## Compliance with ethical standards

**Conflict of interest** The authors declare no conflict of interest in this study.

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