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***Cryptosporidium parvum* among Cancer and Hemodialysis Patients in Ibb City, Yemen: Prevalence and Risk Factors**

Wadee Abdullah Al-Shehari^{1,2}, Eglal Ahmed Qasem¹, Wadhah Hassan Edrees^{3,4*}, Mohammed Sadeq Al-Awar^{4,5}, Alariqi Reem⁶.

¹Department of Microbiology, Faculty of Medical Sciences, Ibb University, Yemen.

²Department of Microbiology, Harbin Medical University, China.

³Medical Microbiology Department, Faculty of Applied Science, Hajjah University, Yemen.

⁴Medical Laboratory Department, College of Medical Sciences, Al-Razi University, Yemen.

⁵Department of Biology, Faculty of Education, Amran University, Yemen.

⁶Medical Laboratory Department, Faculty of Medicine and Health Sciences, Amran University, Yemen.

Abstract:

Background: *Cryptosporidium parvum* is an opportunistic gastrointestinal parasite that cause serious problems for immunocompromised patients. **Aims:** This study aimed to report on the prevalence of *C. parvum* among cancer and hemodialysis patients attending cancer and dialysis centers at Al-Thawra hospital in Ibb city, Yemen. **Methods:** This study is a cross-sectional study conducted among 60 patients with cancer and hemodialysis patients during the period from March to September 2020. The stool specimen was from each patient and *C. parvum* was screened by using formalin-ether sedimentation and modified Ziehl-Neelsen staining. The required data were surveyed by a structured questionnaire. **Results:** Out of 60 stool specimens, only 49(81.7%) were positive for *C. parvum* infection. The cancer patients had more rate of *C. parvum* (90%) than hemodialysis patients (73.3%). Also, the highest rate of *C. parvum* was observed among male participants with cancer (95%) and hemodialysis (76.9%) diseases. The higher frequency of infection was among hemodialysis patients in the age group of 31-40 years. The cancer patients coming from rural areas and hemodialysis patients coming from urban areas had a higher rate of *C. parvum* infection. the majority of patients drinking from well water were positive for *C. parvum* infection. Both cancer and hemodialysis patients with poor personal behavior were more exposed to *C. parvum* infection. Diarrhea, abdominal pain, malaise, poor appetite, nausea, and fever were the most frequent clinical features presented among cancer and hemodialysis patients. Similarly, all cases were completely (100%) found to be suffering from recurrent diarrhea. **Conclusion:** It can be concluded that health education and awareness programs should be implemented directing immunocompromised individuals for preventing and controlling the transmission of opportunistic parasites.

Keywords: *Cryptosporidium parvum*, Ibb City, Cancer, Hemodialysis Patients, Yemen.

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Address for Correspondence:

Dr. Wadhah Hassan Edrees: Medical Laboratory Department, College of Medical Sciences, Al-Razi University, Yemen, **Tel-** +967-778555695; **E-mail:** wadah.edrees@alraziuni.edu.ye, edrees2020@gmail.com.

Introduction

Cryptosporidium parvum is a small protozoan with global distribution and is predicted to be the highest frequent among children, particularly in developing countries. It infects gastrointestinal epithelium cells and exists intracellular in vertebrates especially humans^{1,2}.

Cryptosporidium infection worldwide was found to be the second after rotavirus as a leading cause of diarrhea and deaths among children. In developing countries, it was estimated between 10-15% caused diarrhea among humans. It is responsible for about 30–50% of deaths in infants and children occurring worldwide. *C. parvum* and *C. hominis* are generally responsible for more than 90% of all cases^{2,3}.

The spreading of this parasite mostly via numerous transmission routes that include direct contact with infected persons (person-to-person transmission) or animals (zoonotic transmission); and ingestion of contaminated water (waterborne transmission) or food (foodborne transmission)⁴.

Cryptosporidium causes watery diarrhea which might be occasionally teeming and prolonged⁵. The additional signs include low-grade temperature, intestinal pain, nausea, and vomiting and occasionally headache, anorexia, myalgia, malaise, and faintness¹.

Cryptosporidium infects both immunocompetent and immunocompromised individuals. Cryptosporidiosis, in immunocompetent individuals, is benign and self-limiting, however, it is a major cause of acute and persistent diarrhea with significant morbidity and mortality in immunocompromised patients^{6,7}.

Globally, the prevalence rate of cryptosporidiosis among immunocompetent individuals ranged from 0.1–9.1% in industrialized countries and 2.98–25.9% in developing countries^{8,9}. Also, in the Arabic counties, the *Cryptosporidium* was reported; 4.5% in Qatar¹⁰, 58% in Najaf city, Iraq¹¹, and 1–50% in Yemen^{12,13,14}.

However, several reports have well been documented the frequency of *C. parvum* parasite among immunocompromised patients worldwide. It was recorded; 80% in Iran¹⁵, 8.1–70.3% in Saudi Arabia^{16,17}, 13% in Poland¹⁸, 15–66% in Egypt^{19,20}, 11% in Jordan²¹, and 13.33% in China²².

Yemen is one of the poorest developing countries where opportunistic parasitic infections are widely distributed and easily transmission between

individuals resulting from inadequate supply of drinking water, inadequate environmental sanitation, absence of a sanitary system, and lack of hygienic practices²³⁻²⁸.

The previous studies carried out in different regions of Yemen were focused on intestinal parasitic infections among immunocompetent individuals²⁹⁻³².

Scarce data about the prevalence of cryptosporidiosis among immunocompromised individuals in Yemen.

There are only studies that found the *C. parvum* infection among immunocompromised individuals in Yemen; 27.5% in Sana'a city³³, and 71.26% in Ibb city³⁴. Consequently, this study aimed to report on the prevalence of *C. parvum* among cancer and hemodialysis patients attending cancer and dialysis centers at Al-Thawra hospital in Ibb city-Yemen.

Materials and Methods

Study design and period

The present study was conducted among 60 patients with cancer and hemodialysis patients (30 persons each) aged between 5 to 65 years who recurrent in Al-Thawra hospital in Ibb city-Yemen from March to September 2020.

Data collection

A pre-tested questionnaire was used to collect relevant information from each study participant enrolled in this study. The information data like gender, age, resident area, clinical information representing the type of diarrhea diseases and environmental factors such as drinking water source, personal behavior, and contact with domestic animals were gathered via direct interviews with patients.

Specimens collection and examination

The stool specimen was collected for each patient in a dry, sterile, leak-proof container (60 mL) under aseptic conditions and transported to a medical laboratory for parasite identification. The specimens were immediately processed and examined by microscopic examination of smear prepared from formalin-ether fixed and stained with the modified Ziehl-Neelsen staining techniques as described by Garcia³⁵.

Ethical considerations

The ethical statement of this work was approved by the Ethical Committee of the College of Applied

Science, Ibb University and the hospital of Al-Thawra in Ibb city. The goals of this work were orally explained to all healthcare staff and participants before starting data collection. All participants who enrolled in this study signed the written consent.

Data analysis

The obtained data were entered into an Excel program and analyzed for categorical variables such as frequencies and percentages.

Results

Socio-demographic characterization

In the present study, most stool specimens were collected from a male (55%), age group more than 50 years (25%), coming from urban areas (51.7%), drinking from piped water (66.7%), having a good of personal hygiene (73.3%), food sanitation (61.7%), nutrition status (63.7%), and contact with domestic animals (55%) that summarized in Table (1).

Table 1. Scio-demographic characteristic of subject study

Variables	Categories	Examined No. (%)
Gender	Male	33 (55.0)
	Female	27 (45.0)
Age (in years)	<10	3 (5.0)
	11-20	3 (5.0)
	21-30	12 (20.0)
	31-40	14 (23.3)
	41-50	13 (21.7)
Residence	>50	15 (25.0)
	Urban	31 (51.7)
Source of drinking water	Rural	29 (48.3)
	Piped	40 (66.7)
Personal hygiene	Wells	20 (33.3)
	Good	44 (73.3)
Food sanitation	Poor	16 (26.7)
	Good	37 (61.7)
Nutrition status	Poor	23 (38.3)
	Good	38 (63.3)
Contact with animals	Yes	22 (36.7)
	No	33 (55.0)
	No	27 (45.0)

Prevalence of *C. parvum* infection

This result found that the overall rate of *C. parvum* infection was 49(81.7%) among study subjects. It was observed that most cancer and hemodialysis patients

were infected by *C. parvum* parasite at 27(90%) and 22(73.3%), respectively, as figured in Fig. (1).

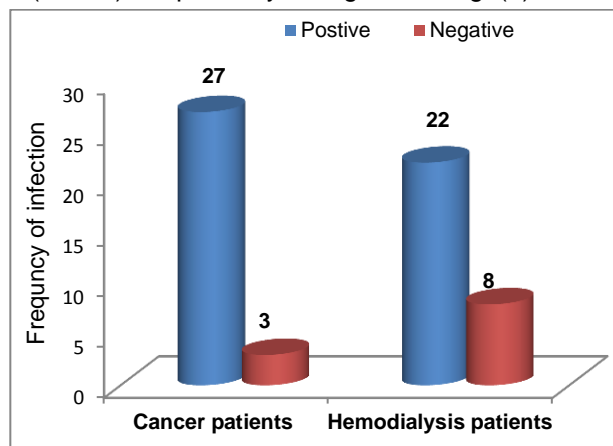


Figure 1. Frequency of *C. parvum* infection among study subjects

Risk factors associated to *C. parvum* infection

This result showed that the highest rate of *C. parvum* was 95% and 76.9%, respectively, among male participants with cancer and hemodialysis diseases. According to age, it was found that the higher rate of infection was among most the age groups of participating cancer patients except age group 21-30 years. Whereas the highest rate was (80%) among the age group 31-40 years with hemodialysis patients followed by 21-30 years, 41 to >50 years, and 11-20 years. The cancer patients coming from the rural area showed a higher rate of *C. parvum* infection than patients coming from the urban area. Whereas, a higher rate of *C. parvum* was reported among hemodialysis patients coming from urban areas. Also, the highest rate of *C. parvum* infection was recorded among patients drinking from well water summarized in Table (2).

Table 3 shows that both cancer and hemodialysis patients with poor personal hygiene were more exposed to *C. parvum* infection as summarized in Table (3).

The results in relation to clinical features accompanied by *C. parvum* infection observed that all patients (100%) presented with diarrhea, 70.3% with abdominal pain, 63% for each with malaise and poor appetite, and the lowest rate was 37% for the presence of fever among cancer patients. In addition, the highest rate of clinical features was diarrhea with 100% and the lowest was vomiting with 72.7% among hemodialysis patients (Table 4).

Table 2. Distribution of *C. parvum* regarding Scio-demographic characterization

Variables	Categories	Cancer patients		Hemodialysis patients	
		Examined No. (%)	Positive No. (%)	Examined No. (%)	Positive No. (%)
Gender	Male	20(66.7)	19(95)	13 (43.3)	10(76.9)
	Female	10(33.3)	7(70)	17(56.7)	12(70.6)
Age (in years)	<10	3 (10)	3(100)	0(0)	0(0)
	11-20	1 (3.3)	1(100)	2 (6.7)	1(50)
	21-30	3 (10)	1(33.3)	9 (30)	7(77.8)
	31-40	4 (13.3)	4(100)	10(33.3)	8(80)
	41-50	7 (23.3)	7(100)	6 (20)	4(66.7)
	>50	12(40)	11(91.7)	3 (10)	2 (66.7)
Residence	Urban	20(66.7)	17(85)	11 (36.7)	10 (90.9)
	Rural	10(33.3)	10(100)	19 (63.3)	12(63.2)
Source of drinking water	Piped	25 (83.3)	22(81.5)	15 (50)	10(66.7)
	Wells	5 (12.7)	5(100)	15 (50)	12(80)

Table 3. Distribution of *C. parvum* among study subjects regarding personal behavior

Variables	Categories	Cancer patients		Hemodialysis patients	
		Examined No. (%)	Positive No. (%)	Examined No. (%)	Positive No. (%)
Personal hygiene	Good	20(66.7)	18(90)	24 (80)	17(70.8)
	Poor	10(33.3)	9(90)	6 (20)	5(83.3)
Food sanitation	Good	13 (43.3)	12(92.3)	24 (80)	17(70.8)
	Poor	17(56.7)	15(88.2)	6 (20)	5(83.3)
Nutrition status	Good	14 (46.7)	12(85.7)	24 (80)	17(70.8)
	Poor	16 (53.3)	14(75)	6 (20)	5(83.3)
Contact with animals	Yes	9 (30)	8(88.9)	24 (80)	19(79.2)
	No	21 (70)	19(90.5)	6 (20)	3(50)

Table 4. Clinical features among infected patients

Variables	Cancer patients	Hemodialysis patients
	No. (%)	No. (%)
Diarrhea	27(100)	22 (100)
Abdominal pain	19(70.3)	21(95.5)
Vomiting	12(44.4)	16(72.7)
Nausea	16(59.2)	20(90.9)
Fever	10(37)	20(90.9)
Weight loss	13(48)	19(86.4)
Poor appetite	17(63)	20(90.9)
Malaise	17(63)	21(95.5)

Table 5 reveals the frequency of diarrhea among patients infected by *C. parvum* infection. Semi-liquid diarrhea (63%) and watery diarrhea (59%), respectively, were the most reported among

participating cancer and hemodialysis patients. Also, it was noticed that all patients completely (100%) suffered from the recurrent diarrhea manifestation, while chronic diarrhea was 48% and 9% lower recorded, respectively, among cancer and hemodialysis patients.

Table 5. Type of diarrhea among infected patients

Variables	Categories	Cancer patients (n=27)	Hemodialysis patients (n=22)
		No. (%)	No. (%)
Type of diarrhea	Watery	10(37)	13(59)
	Semi liquid	17(63)	9(40.9)
	Bloody	8(30)	10(45.5)
Diarrheal manifestation	Chronic	13(48)	2(9)
	Acute	14(52)	20(90.9)
	Recurrent	27(100)	22(100)

Discussion

Cryptosporidium spp. has been well documented as an important cause of chronic diarrhea worldwide among immunocompromised patients. The present finding documented that the overall rate of *C. parvum* prevalence among cancer and hemodialysis patients was 81.7%. This result is higher than earlier reports reported among immunocompromised patients at 7% in Egypt³⁶, 8.1% in Saudi Arabia¹⁶, 11.3% in Turkey³⁷, 27.5% in Sana'a city³³, and 71.26% in Ibb city, Yemen³⁴.

The higher rate noticed in this study may be due to the bad circumstance in Yemen resulting from war since 2015 and so on that increased the poverty rate, and destroyed health infrastructure. Furthermore, the environmental factors, personal habitats, and the patient's immune state are factors contributing to *C. parvum* prevalence in Yemen^{38,39,40,41}.

This finding showed that the patients with cancer had a higher rate of *C. parvum* infection (90%) when compared to hemodialysis patients (73.3%). This is in line with a report by Baqai *et al.*¹⁵ found that *Cryptosporidium* infection was 80% recorded among cancer patients and 35% in dialysis patients.

This result showed that the highest rate of *C. parvum* was recorded among male participants with cancer and hemodialysis diseases. This finding is in agreement with the report of Sayal¹¹ in Iraq, El-kady *et al.*²⁰ in Egypt, Zueter *et al.*²¹ in Jordan. It was proven that the male gender is more susceptible to *Cryptosporidium* spp. infection than the female gender⁴².

In the current result, it was found that the higher rate of infection was among most of the age groups of participating cancer patients except the age group 21-30 years. While the highest rate was 80% among the age group 31-40 years with hemodialysis patients. A similar study found that age groups less than 10 years are more susceptible to *Cryptosporidium* parasite infection resulting from many factors including inadequate hygienic practices, staying for long-time outdoors and playing in contaminated soil, and their undeveloped immune state^{11,43,44,45}.

However, it was observed that the cancer patients coming from rural areas and hemodialysis patients coming from urban areas had a higher rate of *C. parvum* infection. Numerous previous surveys have been shown the high rate of *Cryptosporidium* infection among cases coming from rural areas^{13,46}.

The presence of domestic animals, unsafe drinking water, absence of a sanitary system, and lack of hygienic practices are factors that increase the prevalence of *Cryptosporidium* parasites in rural areas.

It was noticed that the patients drinking from well water were found to be more infected *C. parvum*. This finding is in line with previous reports that showed that unsafe water is a source of pathogenic parasites^{47,48}.

People in Yemen, particularly in rural areas, are usually depending on surface water as the main source of drinking water and home use. So, these water are at risk for parasite contamination resulting from human and domestic animals face during the rainy season^{49,50,51}.

As regards the personal behavior in this study, it was found that cancer and hemodialysis patients with inappropriate personal behaviors had a higher rate of *C. parvum* infection. This finding is in agreement with some studies that reported that inadequate hygienic practices contributed to the prevalence of intestinal parasitic infection among study individuals^{29,52}.

According to clinical features, this result showed that diarrhea and abdominal pain were the most clinical features frequently presented among cancer patients infected by *C. parvum*. In addition, diarrhea (100%), abdominal pain and malaise (95.5% for each), nausea, fever, and poor appetite (90.9% for each) were the most clinical features frequently presented among hemodialysis patients infected by *C. parvum*. These results are in agreement with a study that reported that diarrhea, malaise, poor appetite, and abdominal pain were the most clinical features presented among immunocompromised infected by *Cryptosporidium* infection^{17,46,34}.

These findings were in line with different reports that recorded that acute and persistent diarrhea, abdominal pain, fever, and weight loss were the most observed clinical features significantly associated with *Cryptosporidium* infection^{17,46}.

The present work noticed that semi-liquid diarrhea and watery diarrhea, respectively, were the most observed among participating cancer and hemodialysis patients. Also, it was found that all participating patients completely (100%) suffering from recurrent diarrhea. This is in line with the investigation that found that semi-liquid diarrhea (90.3%) and recurrent diarrhea (100%) were the most type of diarrhea most observed clinical features

significantly associated with *C. parvum* infection among immunocompromised patients³⁴.

The association between diarrhea and *Cryptosporidium* infection has been well documented. The infection by *Cryptosporidium* parasite causes fleeting destruction of microvilli and crypt hyperplasia with inflammatory cell infiltration and quickly recovered in individuals with a competent immune system. Whereas infections can lead to chronic diarrhea, water-electrolyte imbalances, malnutrition, and even death among underdeveloped or compromised immune systems^{5,53}.

Limitations

The limitation of the present work is representing the small sample size. Also, the use of Modified Ziehl-Neelsen stain is an old technique and not well effective to determine parasites. In addition, the lack of advanced techniques like enzyme-linked immunosorbent assay (ELISA) to screen the antigen in stool is another limitation of this work.

Conclusion

In conclusion, the high-rate prevalence of *C. parvum* among cancer and hemodialysis patients can threaten their lives due to persistent diarrhea. Therefore, health education and awareness programs should be implemented directing cancer and hemodialysis patients to control and prevent disease transmission. Further large-scale studies should be performed to find out the other causes of diarrhea, such as other parasites, bacteria, and viruses, among immunocompromised patients.

Conflict of interest

No conflict of interest is associated with this work.

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خفية الأبواغ الصغيرة بين مرضى السرطان والغسيل الكلوي في مدينة إب، اليمن: الانتشار وعوامل الخطر

الملخص

الخلفية: خفية الأبواغ الصغيرة هو طفيلي معوي انتهازي يسبب مشاكل خطيرة للمرضى ذوي المناعة الضعيفة. **الأهداف:** هدفت هذه الدراسة إلى الإبلاغ عن انتشار خفية الأبواغ الصغيرة بين مرضى السرطان والغسيل الكلوي الذين يترددون على مراكز السرطان والغسيل الكلوي في مستشفى الثورة بمدينة إب، اليمن. **الطريقة:** هذه الدراسة عبارة عن دراسة مقطعية أجريت بين 60 مريضاً بالسرطان والغسيل الكلوي خلال الفترة من مارس إلى سبتمبر 2020. تم جمع عينات البراز من كل مريض وتم فحص خفية الأبواغ الصغيرة باستخدام ترسيب الفورمالين-إيثر وصبغة زيهل-نيلسن المعدلة. تم جمع البيانات المطلوبة من خلال استبيان منظم. **النتائج:** من بين 60 عينة براز، كانت 49 (81.7%) منها إيجابية للإصابة بخفية الأبواغ الصغيرة. كان معدل الإصابة بخفية الأبواغ الصغيرة أعلى بين مرضى السرطان (90%) مقارنة بمرضى الغسيل الكلوي (73.3%). كما لوحظ أعلى معدل للإصابة بخفية الأبواغ الصغيرة بين المشاركين الذكور المصابين بالسرطان (95%) وأمراض الغسيل الكلوي (76.9%). كان التكرار الأعلى للإصابة بين مرضى الغسيل الكلوي في الفئة العمرية من 31-40 عامًا. كان مرضى السرطان القادمون من المناطق الريفية ومرضى الغسيل الكلوي القادمون من المناطق الحضرية لديهم معدل أعلى للإصابة بخفية الأبواغ الصغيرة. كانت الغالبية العظمى من المرضى الذين يشربون من مياه الآبار إيجابيين للإصابة بخفية الأبواغ الصغيرة. كان كل من مرضى السرطان والغسيل الكلوي الذين لديهم سلوكيات شخصية ضعيفة أكثر عرضة للإصابة بخفية الأبواغ الصغيرة. كانت الإسهال، وآلام البطن، والشعور بالضيق، وفقدان الشهية، والغثيان، والحمى هي الأعراض السريرية الأكثر شيوعًا التي ظهرت بين مرضى السرطان والغسيل الكلوي. وبالمثل، وجد أن جميع الحالات (100%) تعاني من إسهال متكرر. **الاستنتاج:** يمكن الاستنتاج بأن برامج التنقيف الصحي والتوعية يجب أن تُنفذ لتوجيه الأفراد ذوي المناعة الضعيفة لمنع والسيطرة على انتقال الطفيليات الانتهازية.