REPUBLIC OF TURKEY
VAN YUZUNCU YIL UNIVERSITY
HEALTH SCIENCE INSTITUTE

INVESTIGATION OF *BLASTOCYSTIS* SP. FREQUENCY IN IMMUNOCOMPRAMISED PATIENTS

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DEPARTMENT OF PARASITOLOGY
(MEDICAL PROGRAM)
MASTER'S THESIS

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II

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1. INTRODUCTION

Blastocystis sp. Alexief, 1911 are a protozoan parasite, enteric, anaerobic and eukaryotic. *Blastocystis hominis* was first described in 1912 by Brumpt as a most widespread parasite that inhabits in the gastro-intestinal tract of humans and great group on animals (reptiles, birds, and arthropods). The protozoon can be seen easily in the stool specimen of symptomatic and asymptomatic individuals (Zierdt, 1991; Ozcel et al., 2007; Beyhan et al., 2015).

B.hominis is morphologically classified into six types, vacuolar, multivacuolar, avacuolar, granular, amoeboid, and cyst forms. The cyst phase has been well-considered as a dominant phase that can be seen in surrounding environments (Yamada and Yoshikawa, 2012).

Debates about its effects on immunocompetent and immunocompromised individuals of *B.hominis* are still continuing. Particular group of population have a greater risk of infection by parasite which include imunocompromised and adolescent set. *B.hominis* has a high prevalence that varies between countries and also among different communities of the some countries. In developing countries, the parasites have a higher prevalence (30-50%) in comparison with developed countries (1.5-10%). Prevalence of this parasite is associated with poor hygiene, contact with animals, and consumption of contaminated water or food (Beyhan et al., 2015; Sirria et al., 2015; Robyn, 2015; Rasti et al., 2017).

The pathogenicity of *B.hominis* is still controversial today. According to the reports of some researchers *Blastocystis* sp. are considered as a commensal parasite and others consider as a pathogenic organism. Until now, the researchers have not been convinced that this parasite is the cause of intestinal infection, but there was reported that this parasite infection has been related with diarrhea, fever, anorexia, nausea, urticaria, abdominal cramp, flatulence, discomfort, vomiting, and irritable bowel syndrome (IBS). Blastosystosis might be acute or chronic (Yahya, 2015; Beyhan et al., 2015).

In diagnosis Lugol's iodine, giemsa and trichrome staining are the most popular methods for the parasite detection, and trichrome staining is the most appropriate method for identification. In the presence of five or more parasites in per microscope field and no other pathogenic agent, the patient is considered positive for this parasite. Molecular techniques, ELISA, and stool culture are alternative methods for identify parasites (Ozcel et al., 2007; Tan, 2008; Beyhan et al., 2015; Yahya, 2015).

The objective of the present study was to determine the prevalence of *Blastocystis* sp. in patients with cancer (CA), diabetes mellitus (DM) and chronic renal failure (CRF) and to demonstrate the significance of blastocystosis in these patients.

2. GENERAL INFORMATION

2.1. Historical Review

*B.hominis*is is a parasite that lives in the intestine of human and wide range of animals. It appears that there is a complicated history of this parasite in the literature. Due to the confusion and lack of old scientific data, the exact definition of the parasite has not been clear for a long time (Senay, 1990).

Aleksandrovich Losch had discovered *B.hominis* in 1849 but it has not a evidence for his discovery. Perroncito provided a sufficient written description of *B.hominis*, however he has no illustration associated with this parasite. He denoted that the parasite was likely a member of Coccidia. In 1899, Perroncito again did not have enough documentation about parasites to work, so he could not draw parasites either. In 1899 Borini et al. during study in Perroncito's laboratory, they mentioned as a Perroncito's parasite called it protozoan as well as a corpuscle. There was also no illustration (Zierdt, 1991; Stenzel and Boreham, 1996; Alfellani, 2012; Mehlhorn et al., 2012).

The first name of *Blastocystis*, *Blastocystis enterocola* (1911), a yeast was given by Alexeiff. His appelation is prior to that of Brumpt, who in 1912 coined the name *B. hominis*, changing the specific epithet from enterocola to hominis. There was a belief that Brumpt's classification had priority because he worked only with human material had an early influence. *B.hominis* name is now precisely recognized worldwide. Isolation of the parasite has been approved only in human, monkey, ape, pig, and, perhaps, guinea pig. In 1932 Micheletti used the *Blastocystis* genus that before named by Alexeiff and he added jalinus (actually unknown), named potozoan *Blastocystis jalinus* (Perroncito). After being accepted for a decades, the *B.hominis* has been recapturing of parasitologists till Zeirdt et al.'s studies in 1967 (Zierdt, 1991; Stenzel and Boreham, 1996; Özcel et al., 2007; Alfellani, 2012; Mehlhorn et al., 2012).

2.2. Taxonomy

*B.hominis*is has been described as a protist organism depending on morphologically characteristics. The classification of this parasite is as follows (Charles, 1991; Zierdt, 1991; Stenzel and Boreham, 1996; Özcel et al., 2007; Alfellani, 2012).

Kingdom: Protista
Subkingdom: Protozoa
Phylum: Sarcomastigophora
Subphylum: Sarcodina
Superclass: Rhizopoda
Class: Lobosea
Subclass: Gymnamoeba
Order: Amoebida
Suborder: Blastocystina
Genus: *Blastocystis* Alexief, 1911
Species: *Blastocystis hominis* Brumpt, 1912

2.3. Morphology and Life Cycle

There are fundamentally six different forms of *Blastocystis* sp. that appear in human stool with light microscopy. These forms are vacuolar, avacuolar, multivacuolar, granular, amoeboid, and cyst forms (Tan et al., 2002; Suresh and Smith, 2004; Yamada and Yoshikawa, 2012).

Vacuolar form: This form is also known as vaculated or central vacuole form, and contain a very big vacuole and thin rim of peripheral cytoplasm. Till now the function of central vacuole has not been explained. It has been supposed to act as storage organelle or to act in endodyogeny and schizogony that are two suggested ways of reproduction. This form looks rounded shape with some irregularity in the transmission electron microscopy. Its size is 5-50 μm in diameter. When the organism is cultured, it can grow to a size of more than 50 μm and reaches up more than 200 μm in diameter. According to the contents of vacuolar form morphologically changing is possible. This form is the main form from both xenic and axenic liquid culture. It is reproduced by

binary fission and it contain up to four nuclei that are spaced more or less equally around the cell. The nucleus and cytoplasm present at peripherally of the cell by large central vacuole (Tan et al., 2002; Suresh and Smith, 2004; Tan, 2008; Yamada and Yoshikawa, 2012).

Granular form: According to the reports its size is ranged about 5-19.5 μm. Granular form is usually observed in axenic and monoxenic culture (Zierdt, 1973; Alfellani, 2012). After studying with help of electron microscope three kinds of granular were observed in the cell; metabolic granule, lipid granule, and reproductive granule (Tan and Zierdt, 1973).

There are some similarity and differences between vacuolar and granular forms in terms of the appearance of their central vacuole. Vacuolar form generally contain finely granular that are scattered into vacuole, but the granular form contain granules with different morphological forms. In addition granular form is similar to vacuolar form in having thin bounded cytoplasm surrounding big central vacuole (Dun et al., 1989).

There is lack of information about of having cytolplasmic granule, include lipid granules that could find in the central vacuole and cytoplasm, and reproductive granule in central vacuole. These observations has not been verified (Zierdt, 1973). There is explained myelin like inclusion, small vesicle, lipid droplet, and crystalline granules in the center vacuole of the granular form (Dun et al., 1989).

Amoeboid form: This form of *B.hominis* includes many of disagreements status on its morphology. Size of amoeboid form is well explained approximately between 2.6-7.9 μm in diameter and normally smaller than vacuolar and granular form (Tan, 2008; Alfellani, 2012).

The researchers were reported that amoeboid form appeared less in older culture, cultures that treated with antibiotic, and sometimes in stool sample. There are no central vacuole, one or two nucleus are in the center (Tan and Zierdt, 1973). The amoeboid forms described by Tan and Zierdt (1973) were refuted for the lack of the surrounding membrane around the central vacuole and nucleus. Likewise, Dunn et al. (1989) did not

show a central vacuole, mitochondria, golgi complex, coated pits, and surface coat in their amoeboid description. Tan and Suresh (2006) stated that the organism's outline shape is irregular and folded with one or two large extended pseudopodia. Culture in large amount of serum shows electron lucent granules that spread out into the central of the organism. In most of samples permanent cell wall or membrane are not seen clearly (Tan, 2008; Yamada and Yoshikawa, 2012).

The way of the division of amoeboid cell not approved yet. Some methods of reproduction for this cell have been explained included budding, sporulation, and plasmotomy, but these modes of reproduction had not been supported with any type of conclusive evidences (Tan and Suresh, 2006; Tan, 2008).

Cyst form: The cyst form is the most recently described form of the parasite. This form of the *B.hominis* is smaller than vacuolar and granular form, and approximately about 3-10 μm in diameter. Larger cysts have been isolated from animal hosts. The cyst that isolated from animal fecal is about up to 15 μm in diameter. The distinct feature of this form is the presence of a thick multi-layered cyst wall. In addition to the characteristic cyst wall, the newly formed cysts may in turn be surrounded by the surface coat of the vacuolar form from which they develop or they might lose the surface coat and appear as naked cysts (Stenzel and Boreham, 1996; Özcel et al., 2007; Tan, 2008; Alfellani, 2012; Mehlhorn et al., 2012; Parija and Jeremiah, 2013).

Cyst form contains condensed cytoplasm with many small vacuoles as in other cysts. The cysts isolated from humans are commonly binucleate; however, the number of nuclei can vary from one to four. Mehlhorn explained as up to four nucleuses, Stenzel and Boreham are thought to be only one nucleus per cyst (Mehlhorn, 1988; Stenzel and Boreham, 1991; Parija and Jeremiah, 2013). According subsequent information detected that some time cyst form contain two nuclei. There is no evidence for mode of nuclear division from cyst form. The producing vacuolar form inside the cyst form throughout a multiple fission measured as asexual reproduction method that explained previously but not confirmed (Stenzel, 1995; Tan, 2008).

The cyst form confers protection to the parasite during adverse conditions and is found to remain viable for up to 1 month at 25° C even on exposure to air. The cysts are

now proven to be the transmissible infective forms, which on entering a suitable host develop into vacuolar forms (Parija and Jeremiah, 2013).

Multivacuolar and avacuolar forms:

In the fresh stool or in-vitro cultures, multivacuolar and avacuolar forms are rare and small in size. These forms are mainly characterized by electron microscopy. The multivacuolar form is smaller (approximately 5 to 8 μm in diameter) than the typical vacuolar or granular forms. In multivacuolar forms of *B.hominis* one nucleus is found. Avacuolar forms are smaller (approximately 5 μm in diameter) than *B.hominis* form in culture and did not contain a central vacuole. This form is not surrounded by a surface coat (Dunn et al., 1989; Stenzel and Boreham, 1991; Yamada and Yoshikawa, 2012).

Life cycle: There are many kinds of life cycles and modes of transmission were previously reported by researchers and now it is a little understood (Parija and Jeremiah, 2013; Kumarasamy, 2014). Mode of transmission that suggested is schizogony, plasmotomy, and endodyogeny, were reported by Singh et al. (1995), Tan and Suresh (2007), and Zhang et al. (2007) respectively.

First of all, Alexeieff introduced the life cycle of *Blastocystis.* He confirmed a complex life cycle through binary fission of the binucleate stage (plasmotomic division). Autogamy is asexual to formation cyst. Alexeieff explained that another mode of reproduction is merogony. There was no evidence for illustrating the method of reproduction. Thus binary fission was accepted as a current method of reproduction of the *Blastocystis* (Boreham and Stenzel, 1993).

Human are most possible host of zoonotic subtypes. Already life cycle of the *Blastocystis* has tightly contact with animals. Studies have revealed that suitable hosts could contact *Blastocystis* infection by drinking untreated water or eating raw aquatic plants contaminated with cysts. Recent studies demonstrate that unclean hands can serve as fomites for transmission of cysts from infected individuals on direct contact or from contaminated soil (Özcel et al., 2007; Kumarasamy, 2014).

Upon ingestion, the cysts develop into vegetative forms only in the suitable host. The further continuation of the life cycle depends on the compatibility of the subtype

with the host. The cyst form undergoes excystation in the large intestine to liberate the vacuolar form. The vacuolar forms can transform into any of the other forms. Frequent observations of the amoeboid, avacuolar and multi-vacuolar forms in diarrhea suggest a possibility that these forms might play a role in the pathogenesis (Parija and Jeremiah, 2013).

The life cycle of *B.hominis* is given in detail in the Figure 1.

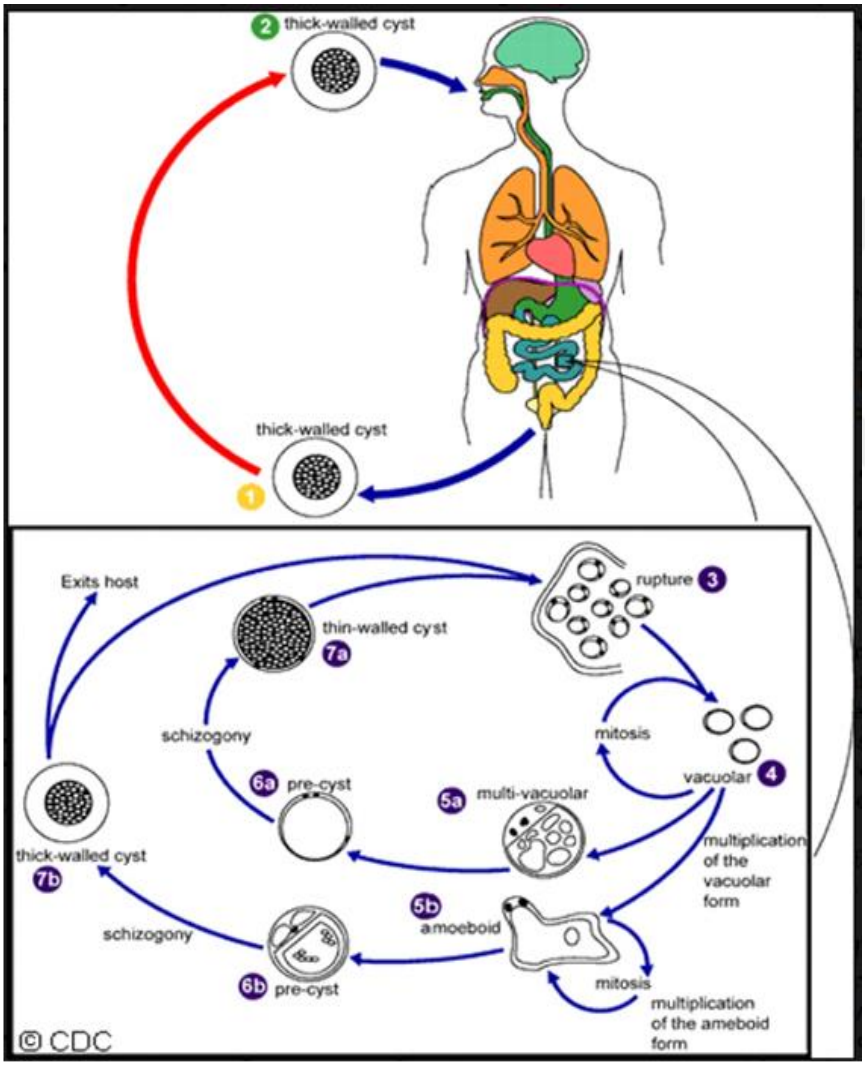

Figure 1. Life cycle of the *B.hominis* (Anonymus, 2017)

The classic form found in human stools is the cyst, which varies tremendously in size from 6 to 40 µm **(1).** The thick-walled cyst present in the stools **(1)** is believed to be responsible for external transmission, possibly by the fecal-oral route through ingestion of contaminated water or food **(2)**. The cysts infect epithelial cells of the digestive tract and multiply asexually (**(3)**, **(4)**). Vacuolar forms of the parasite give origin to multivacuolar **(5a)** and ameboid forms **(5b)**. The multivacuolar develops into a precyst **(6a)** that gives origin to a thin walled cyst **(7a)**, thought to be responsible for autoinfection. The ameboid form gives origin to a precyst **(6b)**, which develops into thick walled cyst by schizogony **(7b)**. The thick walled cyst is excreted in stool **(1)**.

The vacuolar forms encyst in the intestinal lumen to form cysts which are shed in the stool for further transmission. Various authors have claimed to have observed either of the modes of reproduction such as binary fission, budding, plasmotomy, multiple fission, endodyogeny and schizogony. Binary fission of the vacuolar forms is the most commonly observed and well established mode of reproduction. Earlier observations and assumptions of the existence of thick and thin walled cysts which undergo multiple fission to release the progeny are inconclusive due to the lack of scientific evidence (Parija and Jeremiah, 2013).

2.4. Epidemiology

Blastocystis sp. is frequently most common parasite that found in the stool samples of both symptomatic and asymptomatic individuals. This parasite was reported from developing countries (30-50%) more than developed countries (1.5-10%). However there is no enough study for detecting certain rate of prevalence of the *B.hominis* infection in humans (Senay and MacPherson, 1990; Stenzel and Boreham, 1996).

Blastocystis was noticed as being related with diarrhea in tropic and subtropic regions. While some authors say that traveling to the tropics might not be risk factors of infection, others see this factor as a risk factor. Some reports show that blastocystosis is common in resident of tropic, subtropic and developing countries (Alfellani, 2012).

Different various reasons including poor socioeconomic conditions, overcrowding, poor education, and low standard of sanitation and hygiene are cause the high prevalence of *Blastocystis*. Studies have shown that gender has not been a major influence on the prevalence of this parasitosis. Some studies showed that the occurrence of *B.hominis* in adult females is slightly higher than adult males. Incidence of the parasites is a little association with weather conditions. According to the some researchers, this infection is more common in hot conditions than cold weather. Also peoples are mostly travel in summer season from different countries especially to tropic countries where level of hygiene is low (Charles, 1991; Stenzel and Boreham, 1996; Alfellani, 2012).

2.5. Pathogenicity and Clinical Signs

In many studies had made, the pathogenicity of *B.hominis* remained controversially (Zierdt, 1991). This parasite is evaluated as truly pathogen or opportunistic, or pathogenic in certain conditions. *Blastocystis* sp. could be seen from both symptomatic and asymptomatic individuals. This parasite is considered pathogenic, when pathogenic parasites such as *Entamoeba histolytica* and *Giardia intestinalis* in the stool samples are not detected and this agent is 5 or more than 5 in each microscope field (Haider et al., 2013; Robyn, 2015).

Blastocystis sp. is acceptable as a reason for many different diseases or measured as intestinal pathogen, that has obvious relationship with IBS, patients with low immune system (immunosuppressed) including hypoalbuminemia and anasarca, acute and chronic urticaria, cancer and HIV/AIDS. Percentages of prevalence, symptoms and rate of the pathogenicty of the *Blatocystis* are tightly related to the different environmental factories like geography, seasonal factor and genetic diversity (Haider et al., 2013).

The proteases and other hydrolytic enzymes secreted by *Blastocystis* have been identified by polyacrylamide gel electrophoresis and attributed to be responsible for the pathogenesis of gastrointestinal system. Attempts have been made to deduce the functions of these extra-cellular virulence factors by in-vitro studies. *Blastocystis* culture lysates have been found to produce cytoskeletal alterations and induce apoptosis in epithelial cells, which results in increased permeability. Cysteine proteases secreted by the organism are known to stimulate the intestinal mucosal cell to produce interleukin-8. These mechanisms are suggested to be responsible for the fluid loss and intestinal inflammation in affected individuals. The researchers have observed the ability of a cysteine protease to cleave human secretory Ig A thereby helping in immune evasion and promoting parasite survival in-vivo (Parija and Jeremiah, 2013).

The symptoms of gastrointestinal tract by *B.hominis* are usually diarrhea, abdominal cramp, and nausea. The uncomfortable conditions that related to *Blastocystis* infection are fever, diarrhea, some time bloody diarrhea, weakening, abdominal pain, vomiting, dysuria, headache, constipation, and fatigue, are most common symptoms. The patients may have some underlying diseases like ulcerative colitis, breast cancer,

kidney transplant, ulcer, skin itching, heart burn, dizziness. And the main extra intestinal symptoms of blastocystosis are eosinophilia, rectal bleeding, anorexia, fatigue, coetaneous rashes, and *Blastocystis* might be responsible for allergic manifestations (Haider et al., 2013; Beyhan et al., 2015).

2.6. Diagnosis

Microscopy: *B.hominis* forms in microscopically examination could usually be identified easily. The diagnosis of the parasites is the most easily done by native-Lugol method. Also trichrome stain has been used for diagnosis of the *Blastocystis*. Giemsa, gram stain, Wright's stain, and iron hematoxylin are other stains methods that might be successfully used in the diagnosis (Stenzel and Boreham, 1996; Özcel et al., 2007).

Identification of *B.hominis* may sometimes be difficult in wet mount slides, therefore permanent smear is used to be the option method for diagnosis of the organism. The variability from size, shapes, and particular staining of the parasite are confirmed with trichrome and iron hematoxylin. Morphology of the *B.hominis* may change by effects of the environment conditions and in post-treatment stool examination and by effect of osmotic pressure and by long time waiting without fixing of fecal material (Stenzel and Boreham, 1996; Alfellani, 2012).

Morphological forms of the *Blastocystis* sp. are confirmed and enhanced by the help of the transmission electron microscope, especially small cysts because of its contents. However electron microscope has important in researches, and are not used for the routine diagnosis (Stenzel and Boreham, 1996).

Serological diagnosis: In the diagnosis indirect immunofluorescence assay (IFA), and enzyme-linked immune sorbent assay (ELISA) are commonly used. By ELISA method 1/50 threshold dilution was taken as a value for detecting positive results. In particular, specific antibodies are required to identify a small number of *Blastocystis,* and atypical forms. In the a study done by Zierdt (1991) all antigens reacted with vacuole, granular and amoeboid shapes of the parasite were determined with IFA by using rabbit antiserum against whole-cell of the parasites. In other recent studies it was carried out that the serum IgA, secretory IgA, and IgG level presented within positive patients for

B.hominis, in both symptomatic and asymptomatic individuals by ELISA. The study result showed that level of serum IgA, secretory IgA, and IgG in the serum of symptomatic patients is higher than from asymptomatic patients. Especially the level of secretary IgA is higher than humoral IgA (Doğruman Al and Hökelek, 2007; Tan, 2008).

Molecular techniques: Microscopic examination in diagnosis of the *Blastocystis* sp. is generally insensitive, thus molecular techniques such as PCR is used to identification of the parasite. Advantages of PCR techniques are well-known from identification of the parasite. It can be acquired on a stool that remained a long time. PCR technique is faster than both of the formol ethyl acetate concentration technique and culture techniques. This method is suggested for screening for *Blastocystis* infection and detection of prevalence (Stenzvold et al., 2006).

Trichrom staining of direct slide smear with the culture of stool together is the best attempt for isolation and identification of *Blastocystis* species. Isolation of *Blastocystis* sp. DNA from stool or stool culture is more sensitive than from microscopy. PCR is need less time about three hours opposite to culture technique that needs about three to four days. But PCR is not most practicable because of its coast, equipment, and its need for special training compare to trichrom and culture. Integration of all methods of diagnosis and detection are going to give more precision than one diagnostic test alone (Alfellani, 2012).

Concentration techniques: This method is another way that used for detection of the protozoan and other fecal parasites. Researchers have doubt about success of these methods because during centrifugation process may deteriorate each of vacuolar, multivacuolar, and granular forms of the parasite. According to some authors, concentration method is succeed from detection of the *B.hominis.* On the other hand some studied were unbilled to detect *B.hominis* from a fecal material by concentration techniques while *B.hominis* was detected by stained smears of the same fecal material (Alfellani, 2012).

Other diagnostic techniques: Other methods like culture technique, axenization, invasive techniques, and cytological tests are used to detect the *Blastocystis*

species. Invasive techniques were not measured as a routine method for detecting of the *Blastocystis*. Fluid aspirate during endoscopy is used to determination of the parasites in the lumen, cecum. *Blastocystis* sp. is detected by enteral string test in duodenal secretion. Also the infection is diagnosed by touch cytological testing, using endoscopy biopsy of the samples onto clean glass slide and staining with rapid methods like to May-Grunwald-Giemsa. Intestinal infections that associated with *B.hominis* also could be detected by endoscopy and sigmoidoscopy (Charles, 1991; Stenzel and Boreham, 1996; Tan, 2008).

2.7. Treatment and Prevention

Treatment of *Blastocystis* infection has remained controversial. General acceptances, only symptomatic patients with blastocystosis in lack of any other disease are required treatment (Aguiler and Lucia, 2009).

Confirmed treatment procedure includes metronidazole, also known as the first line of therapy for *Blastocystis,* and others are known as a second-choice of drugs that are include trimethoprim-sulfamethoxazole (TMP-SMX), ornidazol, paramomycine, emetine, nitazoxanide, chloroqine, cotrimoxazole, idoquinol, tinidazol, idochlorohydroxyquine, furazolidone, and pentamidine. Drugs used against *Blastocystis* infection are summarized in Table 1 (Aguiler and Lucia, 2009; Coyle et al., 2011).

In symptomatic patients having *Blastocystis* cyst in their stool there may occur coinfection with other pathogens mostly such as *Giardia lamblia, E.histolytica, Entamoeba coli,* and *Dientamoeba fragilis.* If the patient's stool specimens show five or more *Blastocysts* sp. in each microscope field and gastrointestinal symptoms are present in the patient, treatment is recommended in these conditions. In addition, in the absence of other pathogens *Blastocystis* positive patients with IBS or skin rash should be considered for treatment. Based on the available clinical data, metronidazole is usually the most useful medication recommended as a first line of treatment. If metronidazole in not eradicate the organism as usually we look for using TMP-SMX or nitazoxanide or other treatment drugs as a second-line defense (Özcel et al, 2007; Coyle et al., 2011).

Table 1. Drugs and therapeutic schemes available for blastocystosis (Aguilar and Lucia, 2009; Coyle et al., 2011).

Drugs	Age group	Dose
Metronidazole	Adult	750 milligrams thrice daily for 10 days; or 500 milligrams thrice daily for 10 days; or 1.5 grams daily for 7 days
	Pediatric	15 mg/kg twice daily for 10 days or 20-30mg/kg per daily for 10 days
TMP-SMX	Adult	2 double strength tablets daily for 7 days (320 milligrams TMP: 1600 milligrams SMX)
	Pediatric	6 mg/kg TMP and 30 mg/kg SMX daily in two equal doses for 7 days
Nitazoxanide	Adult	500 milligrams twice daily for 3 days
	Pediatric	100–200 milligrams twice daily for 3 days
Tinidazole	Adult	2 grams daily for 5 days
	Pediatric	50 mg/kg/day for 5 days (<40 kg body weight)
Paromomycin		25 mg/kg thrice daily for 10 days 500 milligrams thrice daily for 7 days
Iodoquinol		650 milligrams thrice daily for 10–20 days
Ketoconazole		200 milligrams daily for 14 days
Saccharomyces boulardii (a probiotic)		250 milligrams twice daily for 10 days

Prevention: The transmission mode of the *B.hominis* occurs through contaminated food and water as fecal-oral. Already cyst is infective stage of the parasite. Control measures are good quality of personal hygiene, community safety facilities, and education level. The sensitivity of *Blastocystis* sp. for any sterilization procedures is not confirmed. Some reports have considered that vacuolar and granular form are sensitive to air, oxygen, and desiccation, while not expected that vacuolar and granular forms are act as contamination source for the environment. Cyst remains in the environment and this

form is isolated from sewages. For prevent and control of the *Blastocystis* infection Centers for Disease Control and Prevention (CDC) recommends washing hand before eating and after the toilet, keeping away from infected food and water, wash and peel raw fruit and vegetables before eating, do not drink of tap water when you're travelling. Boiled, chlorinated or bottled water should be used to drink and brush teeth while traveling (Stenzel and Boreham, 1996; Sohail and Fischer, 2005; Haider et al., 2013).

3. MATERIAL AND METHODS

3.1. Material

The study was conducted with a group of patients who were referred to the Parasitology Laboratory from the Yuzuncu Yil University, Faculty of Medicine, Internal Medicine Outpatient Clinic between January 2nd 2017 and September 01st 2017. The patient group included a total of 150 immunocompromised patients (mean age: 54.19±16.74; range: 16-91), of which 69 are female and 81 are male; the control group included 75 healthy individuals (mean age: 46.95±15.15; range: 18-80), of which 34 are female and 41 are male. Twenty-nine individuals in the patient group were younger than 35 and 121 were older 35. This group included 68 cancer (CA) patients, 42 diabetes mellitus (DM) patients, 40 chronic renal failure (CRF) patients. For this study, an approval was obtained from the head of the Yuzuncu Yil University, Faculty of Medicine, Non-Interventional Clinical Research Ethics Committee.

3.2. Methods

Stool samples of the patient and control groups were examined with native-Lugol method. For native-Lugol method, a rice grain size stool sample was taken. Thick smear and thin smear with physiological saline solution and thin smear with Lugol solution were made on the same slide. In the prepared preparation, thick smear was examined with X10 objective for helminth eggs and thin smears were examined with X40 objective for protozoon cysts and trophozoites. Thin smear was stained with a drop of methylene blue when needed. Thus, leukocytes were distinguished from amoebae using the leukocyte staining ability of the methylene blue. The presence of five or more *Blastocystis* sp. in each microscope field at X40 magnification was positivity criterion.

Statistical analysis

Descriptive statistics for the categorical variables were presented as count and percent. Chi-Square test was calculated for determination relationships between the categorical variables. Z test was also used for comparison of proportions. Descriptive statistics for the studied variables (characteristics) were presented as mean, standard deviation, minimum and maximum values. Statistical significance level was accepted as

5% and calculations were conducted using SPSS (ver. 13) and MINITAB (ver. 14) statistical software.

RESULTS

In this study, *Blastocystis* sp. positivity (five or more *Blastocystis* sp.) was detected in 22 (14.7%) patients in the patient group and 3 (4%) individuals in the control group. The highest parasite prevalence was identified in patients with CRF (20%) (Tables 2 and 4). In the stool samples of the parasite positive patients, a second pathogenic parasite was not determined. Four or fewer and five or more *Blastocystis* sp. in each microscopic field in 33 (22%) patient group samples were identified. In this case, *Blastocystis* sp. was determined in 10.7% of the control group samples (Tables 3 and 5).

The highest *Blastocystis* sp. positivity was identified in patients with liver CA (25%) among patients with CA. The positivity rate in other CA patients is presented in Table 6. Vacuolar form was the most common form of parasite in *Blastocystis* sp. positive patients (Table 7). Diarrhea was observed in 27.3% and abdominal pain in 59.1% of the parasite positive patients. Complaints and statistical comparisons of positive and negative cases are presented in Table 8. When the complaints of positive and negative patients in the patient group were compared, it was found that there was a statistically significant difference between the two groups based on presence of abdominal pain ($p= 0.017$).

In the present study, the intestinal parasites were found in 26% of the patient group (33 *Blastocystis* sp. positive patients (Table 3) and 6 positive patients for other intestinal parasites) and in 13.3% of the control group (8 *Blastocystis* sp. positive individuals (Table 3) and 2 positive individual for other intestinal parasites). *G.intestinalis* was identified in three patients (one patient with CRF, two patients with CA), *Entamoeba coli* was identified in two patients (one patient with DM and one patient with CA) and *Chilomastix mesnili* was identified in one patient (CA patient), *Blastocystis* sp. and *E. coli* were identified in one patient (DM patient) in the patient group. In the control group, *G.intestinalis* was detected in one individual and *E.coli* was detected in one individual.

The mean, standard deviation and minimum-maximum values of the ages of the patient and control group members are presented in Table 9. In these 2 groups, the

mean, standard deviation, and min.-max. values of the ages of *Blastocystis* sp. positive individuals based on age are presented in Table 10. Mean number, standard deviation and min.-max. values of the *Blastocystis* sp. determined in the stool of patients who are positive are presented in Table 11. In Table 11, it was observed that the average number of parasites in the patient group was higher when compared to the control group. Mean parasite number was highest in CA patients.

There was a statistically significant correlation based on *Blastocystis* sp. positivity between the immunocompramised patient group (150 patients) and the control group (75 individuals) (p= 0.004). Furthermore, there were significant differences between *Blastocystis* sp. positivity and DM (p= 0.040) and CRF (p= 0.015) (Table 2). There was no statistically significant difference between genders and age groups in the frequency of this parasitic in the patient group (Tables 2 and 4).

When all patients with *Blastocystis* sp. (parasite count: 5≤ and ≤4; Tables 3 and 5) were considered, a statistically significant difference was found between the patient group and control group based on the parasite positivity (p= 0.021). However, a significant correlation was found between the CRF (p= 0.017) and *Blastocystis* sp. positivity (Table 3).

Table 2. *Blastocystis* sp. positivity (the parasite number: 5≤) according to age groups

	Total		**≤35**		**≥36**	
	n/N	%	n/N	%	n/N	%
Patient groups						
CA (*p= 0.146)	7/68	10.3 (**p= 0.558)	2/13	15.4	5/55	9.1
DM (*p= 0.040) [S]	7/42	16.7 (**p= 0.846)	1/7	14.3	6/35	17.1
CRF (*p= 0.015) [S]	8/40	20 (**p= 0.854)	2/9	22.2	6/31	19.4
Total (*p= 0.004) [S]	22/150	14.7 (**p= 0.678)	5/29	17.2	17/121	14
Control group (Healthy People)						
Total	3/75	4	2/18	11.1	1/57	1.8

N: Total number of patients, n: Number of patients who are positive
*Patient group and control group were compared. ** Age groups were compared in the patient group.
[S] p value is statistically significant.

Table 3. *Blastocystis* sp. positivity (the parasite number: ≤4 and 5≤) according to age groups

	Total		≤35		≥36	
	n/N	%	n/N	%	n/N	%
Patient groups						
CA (*p= 0.335)	11/68	16.2 (**p= 0.499)	3/13	23.1	8/55	14.5
DM (*p= 0.079)	10/42	23.8 (**p= 0.757)	2/7	28.6	8/35	22.9
CRF (*p= 0.017) [s]	12/40	30 (**p= 0.697)	2/9	22.2	10/31	32.3
Total (*p=0.021) [s]	33/150	22 (**p= 0.847)	6/29	20.7	27/121	22.3
Control group (Healthy People)						
Total	8/75	10.7	3/18	16.7	5/57	8.8

N: Total number of patients, n: Number of patients who are positive
*Patient group and control group were compared. ** Age groups were compared in the patient group.
[s] p value is statistically significant.

Table 4. *Blastocystis* sp. positivity (the parasite number: 5≤) according to gender

	Total		Female		Male	
	n/N	%	n/N	%	n/N	%
Patient groups						
CA (*p= 0.690)	7/68	10.3	2/29	6.9	5/39	12.8
DM (*p= 0.438)	7/42	16.7	3/24	12.5	4/18	22.2
CRF (*p= 0.871)	8/40	20	3/16	18.8	5/24	20.8
Total (*p= 0.871)	22/150	14.7	8/69	11.6	14/81	17.3
Control group (Healthy People)						
Total	3/75	4	1/34	2.9	2/41	4.9

N: Total number of patients, n: Number of the positive cases
* Genders were compared in the patient group.

Table 5. *Blastocystis* sp. positivity (the parasite number: ≤4 and 5≤) according to gender

	Total		F		M	
	n/N	%	n/N	%	n/N	%
Patient groups						
CA (*p= 0.331)	11/68	16.2	3/29	10.3	8/39	20.5
DM (*p= 0.605)	10/42	23.8	5/24	20.8	5/18	27.8
CRF (*p= 0.729)	12/40	30	4/16	25	8/24	33.3
Total (*p= 0.201)	33/150	22	12/69	17.4	21/81	25.9
Control group (Healthy People)						
Total	8/75	10.7	3/34	8.8	5/41	12.2

F: Female, M: Male, N: Total number of patients, n: Number of the positive cases
* Genders were compared in the patient group.

Table 6. *Blastocystis* sp. positivity according to CA type in the CA patients

	parasite number: 5≤		parasite number: 5≤ and ≤4	
Patient groups	Nr.	%	Nr.	%
Breast CA (n: 7)	1	14.3	1	14.3
Stomach CA (n: 15)	2	13.3	4	26.7
Colon CA (n: 17)	2	11.8	2	11.8
Esophagus CA (n: 3)	--	--	--	--
Prostat CA (n: 5)	--	--	--	--
Liver CA (n: 4)	1	25	1	25
Leukemia (n: 11)	1	9.1	1	9.1
Hodgkin lymphoma (n: 6)	--	--	2	--
Total (n: 68)	7	10.3	11	16.2

n: Total patients, Nr.: Positive number

Table 7. Forms determined in the positive patients (the parasite number: 5≤)

Forms	Nr. (n: 22)	%
Vacuoler	14	63.6
Vacuoler and Granular	6	27.3
Vacuoler and Cyst	1	4.5
Vacuoler, Granular and Cyst	1	4.5

Nr.: Number

Table 8. Complaints of *Blastocystis* sp. positive cases in the patient group

Patients		Diarrhea	Abdominal pain	Nausea	Vomiting	Anorexia	Weight loss	Consti-pation
positive cases	Number (n: 22)	6	13	4	1	7	9	1
	%	27.3	59.1	18.2	4.5	31.8	40.9	4.5
negative cases	Number (n: 128)	23	36	32	8	39	56	7
	%	18	28.1	25	6.3	30.5	43.8	5.5
	p values	0.356	0.006 [s]	0.597	0.730	0.90	0.803	0.85

n: Total patients; [s] p value is statistically significant.

Table 9. Mean, standard deviation and min.-max. values of ages of the patient and the control groups

	n	**Mean**	**SD**	**Min.**	**Max.**
Patient groups					
CA	68	56.47	16.74	18	84
DM	42	53.10	14.86	29	91
CRF	40	51.45	16.43	16	76
Total	100	54.19	16.74	16	91
Control group					
Total	75	46.95	15.15	18	80

n: Number of the positive cases, SD: Standard deviation

Table 10. Mean, standard deviation and min.-max. values of ages of positive cases in the patient and the control group

	n	Mean	SD	Min.	Max.
Patient groups					
CA	7	57.29	24.05	18	81
DM	7	65.43	19.26	30	91
CRF	8	49.88	20.90	16	74
Total	22	57.18	21.44	16	91
Control group					
Total	3	36	14.73	27	53

n: Number of the positive cases, SD: Standard deviation

Table 11. Mean, standard deviation and min.-max. values of *Blastocystis* sp.forms determined in stool samples of the positive cases

Patient group								
n (the parasite number: 5≤)		Mean	Std. dev.	Std. error	95% Confidence interval for mean		Min.	Max.
					Lower Bound	Upper Bound		
CRF	8	10,03	1,87	,66	8,47	11,58	7,80	13,20
DM	7	10,34	3,19	1,203	7,40	13,29	6,40	15,20
CA	7	12,83	3,42	1,29	9,67	15,99	7,20	16,60
Total	22	11,02	3,00	,64	9,69	12,35	6,40	16,60
Control group								
Total	3	7,20	1,06	,61101	4,57	9,83	6,00	8,00

n: Number of the positive cases

5. DISCUSSION AND CONCLUSION

Intestinal parasitosis that caused by *Blastocystis* sp. has also been reported as a clinically important infection in immunocompromised patients. The infection is self-limiting in immunocompetent patients, but it may cause persistent diarrhea and severe malabsorption in immunodeficient patients. This parasite may also play a significant role in several chronic gastrointestinal illnesses such as IBS and inflammatory bowel disease (Özcel et al., 2007; Gil et al., 2013, Wawrzyniak et al., 2013; Darabian et al., 2016).

There are many researches on *B.hominis* frequency in different groups of immunocompromissed patients.

Faidah et al. (2016) have studied on two groups of patients, 139 immunosuppressed and 130 immunocompetent. They have used to wet saline and iodine mounts and modified Ziehl-Neelsen stain methods for stool samples of the patient. In the study parasitic infections among immunosuppressed patients were determined at 43.2%, whereas these infections were positive at 21.5% in the control immunocompetent group. *B.hominis* (33.3%) and *C.parvum* (28.3%) were the most common protozoal infections within immunosuppressed group. There was a significant difference between the two groups: flatulence and abdominal pain were more prevalent in the control group than in immunosupressed patients ($p<0.05$).

In the study done by Abdel-Hafeez et al. (2012) a total of 450 stool samples were collected from clinics of Pediatric Department. The researchers carried out the study on two groups (200 immunosuppressed and 250 immunocompetent children). The stool samples were subjected to wet saline and iodine mounts, acid fast stain and Giemsa stain. Parasitic infections were positive in 94% of immunosuppressed children and 60% of immunocompetent children ($p<0.0001$). In this study it was stated that *B.hominis* was determined in 12.1% of immunosuppressed group and 7.2% of immunocompetent group.

Rasti et al. (2017) have performed a research in Kashan and Qom city of Iran. To this study 265 patients (50 renal transplant recipient (RTR), 20 HIV/AIDS, 135

hemodialysis (HD), and 60 CA patients) were taken. In the study control group consist of 120 healthy individual. Direct smear, concentration technique, agar plate, and Ziehl-Neelsen staining were used for identification. The prevalence of intestinal parasite infection was 11.7% (31/265) in the patient group consisting of HD (11.9%), CA (6.7%), RTR (12%) and HIV/AIDS (25%) patients, while this prevalence was 0% in control group. In the study *B.hominis* was the most common parasite (4.2%). Infection rate was significantly higher in male than female (p= 0.002) (Rasti et al., 2017).

In the present study, *Blastocytis* sp. positivity was found in 14.7% of 150 immunecompromised DM, CA and CRF patients. The statistical comparison between the patient group and the control group in the present study (p= 0.004) was consistent with the findings in a study mentioned above (Abdel-Hafeez et al., 2002). In another study (Faidah el al., 2016), it was found that the rate determined in the patient group was higher than the rate found in our study. In another study mentioned above (Rasti et al., 2017), *B.hominis* positivity in CA and HD patients was lower compared to that in the present study.

In the present study, there was a statistically significant difference between *Blastocystis* sp. positive patients and the patients who were *Blastocystis* sp. negative only based on the clinical symptom of abdominal pain (p= 0.017) This result was consistent with other study findings (Faidah el al., 2016). In our study there is no statistically significant difference between the genders in terms of the parasite positivity, but in a study it was found that this result is statistically significant (p= 0.002; Rasti et al., 2017).

In a study from Alexandria, Egypt, 101 children (54 leukemic immunocompromised patients as the case group and 46 immunocompetent people as the control group) have been enrolled. The researchers have stated that *B.hominis* was detected in 54.5% of immunocompromised and 67.4% of immunocompetent ones (p= 0.223). In addition, there is no statistically significant difference between the gender and age groups in terms of the parasite positivity (Eassa et al., 2016).

In one of the studies, it was studied *B.hominis* frequency in patients with hematological malignancy (HM). In this study the patient group was consisted of 206

patients with HM with gastrointestinal complaints and the control group was consisted of 200 patients without HM, with gastrointestinal complaints. In the HM group, the most common parasite was *B.hominis* (13%). The parasite was detected in 1% of the control group. In the study a statistically significant difference ($p<0.05$) was found between positivity of this parasite and HM. It has been stated that symptoms were non-specific for *B.hominis* in HM patients (Taşova et al., 2000).

In another study *Blastocystis* sp. rate has been examined in the patients with colorectal CA. The researcher determined this parasite in 21.08% of 43 colorectal CA patients as case group, and in 9.95% of 22 peoples as control group (Kumarasamy, 2014).

Yersal et al. (2016) have investigated *Blastocystis* sp. frequency in CA patients. In the study this parasite has been detected in 6.5% of 232 stool samples by microscopy and in 10.8% by culture methods. It was stated that the parasite frequency was higher in the male (19%) than the females (6.5%) ($p<0.05$). The researchers determined that *Blastocystis* sp. was found more frequent in patients with lung CA among CA patients ($p<0.05$).

In a study intestinal parasitosis has been assessed among anticancer chemotherapy patients. The researchers of the study have performed stool examinations a total of 206 patients, aged 3 to 18 years. According to their results the overall rate of intestinal parasites was 63.1% and *C.parvum* was the highest (30.1%) followed by *G.lamblia* (18.0%) and then *Cyclospora cayetanensis* (5.3%). *B.hominis* and *E.histolytica/dispar* were detected in 4.9%, 2.4% respectively. They have stated that the majority of infected patients suffered from diarrhea, and the risk of intestinal parasitosis neither differed significantly with patients' age nor gender (Al-Qobati et al., 2012).

In a study conducted on CA patients stool samples have been collected from 80 non-CA. In addition, 138 CA patients including 74 colorectal CA patients and 64 non-gastrointestinal CA patients were taken from the samples. *B.hominis* was determined in 29.7, 25 and 15% among colorectal CA, non-gastrointestinal CA patients and non-CA patients, respectively (Mohamed et al., 2017).

A study is performed by Boghdady (2017) to show *B.hominis* prevalence in CA patients and healthy individuals. In this study the parasite has been determined in 24% of 50 patients with haematological malignancies treated with chemotherapy, 32% of 50 patients with solid organ tumors treated with chemotherapy, 22% of 50 patients with solid organ tumors treated with radiotherapy, 36% of 50 healthy subjects as control group. However, no statistically significant difference was recorded between different groups.

Although *B.hominis* was detected in 10.3% of 68 CA patients in the present study, no statistically significant difference was found between CA patients and the control group. This result was consistent with statistical results in two previous studies (Eassa et al., 2016; Boghdady, 2017).

Furthermore, no difference was found between the CA patients based on gender and age groups in the present study. In a previous study (Taşova et al. 1999), different statistical results were obtained when compared to our study. In two previous studies conducted on CA patients (Kumarasamy, 2014; Mohamed et al., 2017), higher rates of *B.hominis* was detected when compared to the present study. In two other studies lower rates were determined (Al-Qobati et al., 2012; Yersal et al., 2016).

Limited numbers of studies were conducted to determine the frequency of intestinal parasites or *B.hominis* in patients with DM.

Mohtashamipour et al. (2015) have investigated intestinal parasites frequency in 118 DM patients (patient group) and 118 non-DM individuals (control group). They were examined stool samples of the groups by direct wet smear, the concentration and staining techniques. In the study parasitic infections were detected in 26.3% of DM patients and 6.8% controls group ($p<0.050$). The most detected infection was blastocystosis (n= 14). It was stated that specifically *B.hominis* in intestinal parasites may be a risk factor in patients with DM.

In the study that did by Tangi et al. (2016) they took 150 patients with DM as the patient group and 85 individuals as the control group (non-diabetic). The stool samples were evaluated with direct microscopic method, formalin-ether and Ziehl

Neelsen staining method. In this research *B.hominis* was determined in 10% of patients with DM and 23.5% of non-diabetic group. The statistical evaluation showed that there are a significant different between patients group and control group in the prevalence of *B.hominis*.

In one (Mohtashamipour et al., 2015) of two studies that evaluated the *B.hominis* frequency in patients with DM, statistically significant differences were determined between the patient group and the control group, similar to our findings. In another study (Tangi et al., 2016), lower *B.hominis* rate was detected (10%) when compared to our findings (16.7%).

Only a few studies were conducted on the frequency of *Blastocystis* sp. in patients with CRF.

In a study prevalence rate of intestinal parasite in relate to HD patients was investigated. In this study, 110 HD patients (the patient group) and 86 people (the control group) were evaluated. The researchers found *Cryptosporidium* in 26.4%, *Blastocystis* in 24.5% of this patient group. Blastocystosis was determined in 41.9% of the control group ($p<0.05$). A significant difference between the two groups has been observed with regard to symptoms, with bloating, postprandial fullness, and abdominal pain being more frequent in the control group than in the HD group ($p< 0.05$) (Gil et al., 2013).

Azami et al. (2010) investigated intestinal parasitic infections in the renal transplant recipients (RTR) by using direct smear, concentration and staining methods. In their study 33.3% of 150 renal transplant recipients and 20% of 225 people as the control group were infected with intestinal parasites. The researchers detected *E. coli, Endolimax nana, G.lamblia, Iodamoeba butschlii, C.mesnili* and *A.lumbricoides*. They stated that *Blastocystis* sp. was detected in 4.7% of RTR, 2.2% of the control group.

In a previous study (Gil et al., 2013) conducted with CRF patients, there was a statistically significant difference between the patient group and the control group similar to our findings. In a study (Azami et al., 2010), higher *Blastocystis* sp. positivity rate was found when compared to our results.

To date, *B.hominis/Blastocystis* sp. frequency was evaluated in other immunocompramised patient groups and different results were obtained.

Metha et al. have taken 200 patients that have IBS, ages between 18-55 years. According to their result *B.hominis* were reported in 43% out of 200 patients. In the study it has been stated that the predominant form was vacuolar form (Mehta et al., 2015).

Relationship between IBS (13 to 64 years old) and *B.hominis* has been investigated in a study conducted by Mohemmi et al. (2015). The researcher were selected a total of 81 patients with IBS and 81 patients with other digestive disorders. In this study using the stool culture technique, as the golden standard, infection in 45.67% of the case group and 22.22% of the control group was reported. In addition statistical difference was significant ($p<0.001$).

Darabian et al. (2016) have investigated the association between *B.hominis* and IBS. In this study 100 IBS cases and 100 healthy people were included. It was found that *B.hominis* was positive in 26% of IBS patients, and 9% of control group ($p= 0.002$), *G.lamblia* was positive in 6% of IBS patients, and in none of control participants ($p= 0.01$).

A study has been conducted on the clinical profile of intestinal parasitic infections among immunocompromised children with diarrhea. Forty-two patients were included in this study, mostly aged one to five years (78%) and HIV positive (52%). It was stated that the intestinal parasites were found in 24 (57%) of 42 patients in which *B.hominis* comprised the largest proportion (23/24= 96%) (Idris et al., 2010).

In the present study, we compared the control group with 3 different patient groups. Furthermore, the parasite forms and complaints of the patient were determined in the positive patients and the concentration of *Blastocystis* sp. in stool specimens was determined. In the present study, the patients were considered positive when numerous (5≤) *Blastocystis* sp. were present and at least one *Blastocystis* sp. was present in stool samples.

In the present study, the intestinal parasites were found in 26% of the patient group and in 13.73% of the control group samples. *Blastocystis* sp. positivity (parasite count: 5≤) was statistically significantly different between immunocompromised patients (150 patients) and control group, furthermore, between DM and CRF patients and the control group. The most common complaints in the positive cases were abdominal pain and the most common form was the vacuolar form. It was found that the intensity of *Blastocystis* sp. in the microscopic fields was higher in the patient group when compared to the control group. This highest density was found in CA patients when compared to other patient groups. Based on the study findings, we concluded that blastocystosis should be taken into consideration in immunocompromised patients, especially DM and CRF patients.

SUMMARY

Ismael AA. Investigation of *Blastocystis* sp. Frequency in Immunocompramised Patients. Van Yuzuncu Yil University Institute of Health Sciences, M. Sc. Thesis in Department of Medical Parasitology, Van, 2017. The objective of the present study was to determine the prevalence of *Blastocystis* sp. in patients with cancer (CA), diabetes mellitus (DM) and chronical renal failure (CRF) and to demonstrate the significance of blastocystosis in these patients. The study was conducted with a group of patients who were referred to the Parasitology Laboratory from the Yuzuncu Yil University, Dursun Odabas Medical Center, Internal Medicine Outpatient Clinics between January 2nd 2017 and September 01st 2017. The patient group included a total of 150 immunocompromised patients and the control group included 75 healthy individuals. Twenty-nine individuals in the patient group were younger than 35 and 121 were older 35. This group included 68 CA patients, 42 DM patients, 40 CRF patients. Patient and control group stool samples were examined with native-Lugol method. The presence of five or more *Blastocystis* sp. in each microscope field at X40 magnification was positivity criterion. In the present study, intestinal parasites were found in 26% of the patient group and in 13.3% of the control group. *Blastocystis* sp. positivity (5 and more *Blastocystis* sp. in each field) was determined in 22 (14.7%) patient group samples and 3 (4%) individuals in the control group. The highest prevalence rate of the parasite was identified in patients with CRF (20%). The highest *Blastocystis* sp. positivity was identified in patients with liver CA (25%) among patients with CA. Vacuolar form was the most common parasite form in *Blastocystis* sp. positive patients. There was a statistically significant correlation based on *Blastocystis* sp. positivity between the immunocompramised patient group (150 patients) and the control group (75 individuals) (p= 0.004). Furthermore, there were significant differences between *Blastocystis* sp. positivity and DM (p= 0.040) and CRF (p= 0.015). There was no statistically significant difference between genders and age groups in the frequency of this parasitic in the patient group. When the complaints of positive and negative patients in the patient group were compared, it was found that there was a statistically significant difference between the two groups based on the presence of abdominal pain only (p= 0.017). Based on the study findings, we concluded that blastocystosis should be taken into consideration in immunocompromised patients, especially DM and CRF patients.

Key words: *Blastocystis* sp, Immunocompramised patients, stool examination

ÖZET

Ismael AA. Immunitesi Bozulmuş Hastalarda *Blastocystis* sp. Sıklığının Araştırılması. Van Yüzüncü Yıl Üniversitesi Sağlık Bilimleri Enstitüsü, Tıbbi Parazitoloji Anabilim Dalı Yüksek Lisans Tezi, Van, 2017. Bu çalışmanın amacı kanserli (CA), diabetes mellituslu (DM) ve kronik böbrek yetmezlikli (KBY) hastalarda *Blastocystis* sp. sıklığını belirlemek ve bu hastalarda blastocystosisin önemini ortaya koymaktır. Çalışma 02.01.2017 ve 01.09.2017 tarihleri arasında, Yüzüncü Yıl Üniversitesi Dursun Odabaş Tıp Merkezi Dahiliye Polikliniklerinden Parazitoloji Laboratuarına yönlendirilen bir grup hasta üzerinde yürütüldü. Hasta grubu immunitesi bozulmuş olan toplam 150 hastadan, kontrol grubu ise sağlıklı 75 kişiden oluştu. Hasta grubunda 29 kişi 35 yaşından küçük, 121 kişi 35 yaşından büyüktü. Bu gruba 68 CA'lı, 42 DM'lu, 40 KBY'li hasta dahil edildi. Hasta ve kontrol grubunun dışkı örnekleri nativ-Lugol yöntemi ile incelendi. Pozitiflik kriteri X40 büyütmede her mikroskop alanında beş ya da daha fazla sayıda *Blastocystis* sp. varlığı olmuştur. Bu çalışmada intestinal parazitler hasta grubunun %26'sında, kontrol grubunun %13,3'ünde saptandı. *Blastocystis* sp. pozitifliği (her sahada 5 ve daha fazla sayıda *Blastocystis* sp.) hasta grubuna ait örneklerin 22 (%14.7)'sinde, kontrol grubundaki kişlerin 3(%4)'ünde belirlendi. Parazitin en yüksek prevalans oranı KBY'li hastalarda (%20) tespit edildi. CA'lı hastalar arasında en yüksek *Blastocystis* sp. pozitifliği karaciğer CA'lılarda (%25) saptandı. *Blastocystis* sp. pozitif hastalarda en yaygın olarak görülen form vakuoler formdu. İmmunitesi bozulmuş hasta grubu (150 hasta) ile kontrol grubu (75 kişi) arasında *Blastocystis* sp. pozitifliği bakımından istatistiksel olarak anlamlı fark belirlendi (p= 0.004). Ayrıca parazitin pozitifliği ile DM (p= 0.040) ve KBY (p= 0.015) arasında da önemli farklar saptandı. Hasta grubunda bu parazitin sıklığı bakımından yaş grupları ve cinsiyetler arasında istatistik olarak anlamlı fark yoktu. Hasta grubunda pozitif ve negatif bulunan hastaların şikayetleri karşılaştırıldığında, iki grup arasında sadece karın ağrısı bakımından istatistik olarak anlamlı fark bulundu (p= 0.017). Çalışmamızın bulguları dikkate alındığında, başta DM ve KBY'li hastalar olmak üzere immunitesi bozulmuş hastalarda blastocystosisin dikkate alınması gerektiği sonucuna varıldı.

Anahtar Kelimeler: *Blastocystis* sp., İmmunkompramize hastalar, dışkı bakısı

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CURRICULUM VITAE

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ATTACHMENTS

Attachment 1. Ethical Approval Paper (Page 1)

T.C.
YÜZÜNCÜ YIL ÜNİVERSİTESİ
TIP FAKÜLTESİ
GİRİŞİMSEL OLMAYAN
KLİNİK ARAŞTIRMALAR ETİK KURULU
KARAR FORMU

BAŞVURU BİLGİLERİ	ARAŞTIRMANIN AÇIK ADI	İmmünitesi bozulmuş hastalarda Blastocystis sp. sıklığının araştırılması			
	ARAŞTIRMA PROTOKOL KODU	Yok			
	KOORDİNATÖR/SORUMLU ARAŞTIRMACI UNVANI/ADI/SOYADI	Doç.Dr. Zeynep TAŞ CENGİZ			
	KOORDİNATÖR/SORUMLU ARAŞTIRMACININ UZMANLIK ALANI	Parazitoloji			
	KOORDİNATÖR/SORUMLU ARAŞTIRMACININ BULUNDUĞU MERKEZ	Yüzüncü Yıl Üniversitesi Tıp Fakültesi Parazitoloji Anabilim Dalı			
	DESTEKLEYİCİ	Yok			
	DESTEKLEYİCİNİN YASAL TEMSİLCİSİ	Yok			
	ARAŞTIRMANIN TÜRÜ	**Tüm gözlemsel çalışmalar**	☐		
		Anket çalışmaları	☐		
		Dosya ve görüntü kayıtları kullanılarak yapılan retrospektif arşiv taramaları ve benzeri gözlemsel çalışmalar	☐		
		Kan, idrar, doku, görüntü gibi biyokimya, mikrobiyoloji, patoloji ve radyoloji koleksiyon materyalleriyle veya rutin muayene, tetkik, tahlil ve tedavi işlemleri sırasında elde edilmiş materyallerle yapılacak çalışmalar	☐		
		Rutin tetkik ve tedavi işlemleri sırasında elde edilmiş materyallerle yapılacak çalışma	☒		
		Hücre veya doku kültürü çalışmaları	☐		
		Gen tedavisi klinik araştırmaları dışında kalan ve tanımlamaya yönelik olarak genetik materyalle yapılacak araştırmalar	☐		
		Hemşirelik faaliyetlerinin sınırı içersinde yapılacak araştırmalar	☐		
		Gıda katkı maddeleriyle yapılacak diyet çalışmaları	☐		
		Egzersiz gibi vücut fizyolojisi ile ilgili araştırmalar	☐		
		Antropometrik ölçümlere dayalı yapılan çalışmalar	☐		
		Yaşam alışkanlıklarının değerlendirilmesi araştırmaları gibi İnsana bir hekimin doğrudan müdahalesini gerektirmeden yapılacak olan tüm araştırmalar	☐		
	ARAŞTIRMAYA KATILAN MERKEZLER	TEK MERKEZ ☒	ÇOK MERKEZLİ ☐	ULUSAL ☒	ULUSLARARASI ☐

DEĞERLENDİRİLEN DİĞER BELGELER	**Belge Adı**		**Açıklama**
	ARAŞTIRMA BÜTÇESİ	☒	
	BİYOLOJİK MATERYEL TRANSFER FORMU	☐	
	YILLIK BİLDİRİM	☐	
	SONUÇ RAPORU	☐	
	DİĞER:	☒	İyi Klinik Uygulamaları Taahhütnamesi,Tüm Araştırmacılara Ait Özgeçmiş,Anabilim Dalı Yazısı, Literatür ve CD

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ATTACHMENT 1. Ethical Approval Paper (Page 2)

T.C.
YÜZÜNCÜ YIL ÜNİVERSİTESİ
TIP FAKÜLTESİ
GİRİŞİMSEL OLMAYAN
KLİNİK ARAŞTIRMALAR ETİK KURULU
KARAR FORMU

KARAR BİLGİLERİ	**Karar No: 02**	**Tarih: 07.02.2017**
	Doç.Dr. Zeynep TAŞ CENGİZ sorumluluğunda yapılması tasarlanan ve yukarıda başvuru bilgileri verilen **"İmmünitesi bozulmuş hastalarda *Blastocystis* sp. sıklığının araştırılması"** isimli bilimsel araştırma başvuru dosyası ve ilgili belgeler araştırmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiştir. Araştırmacıların Yüzüncü Yıl Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulunun Çalışma Esasları Hakkında Yönergesinde belirtilen hususları yerine getirdikleri belirlenmiş olup, çalışmaları ile ilgili tüm sorumluluk araştırmacılara ait olmak üzere, söz konusu çalışmanın gerçekleştirilmesinde sakınca bulunmadığına, toplantıya katılan Etik Kurul üye tam sayısının salt çoğunluğu/oy birliği ile karar verilmiştir.	
GİRİŞİMSEL OLMAYAN KLİNİK ARAŞTIRMALAR ETİK KURULU		
ETİK KURULUN ÇALIŞMA ESASI	Klinik Araştırmalar Hakkında Yönetmelik, İyi Klinik Uygulamaları Kılavuzu	
BAŞKANIN UNVANI / ADI / SOYADI:	**Prof.Dr. Oğuz TUNCER**	

Unvanı/Adı/Soyadı	Uzmanlık Alanı	Kurumu	Cinsiyet		Araştırma ile ilişki		Katılım *		İmza
Prof.Dr. Oğuz TUNCER	Çocuk Sağlığı ve Hastalıkları	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Yrd.Doç.Dr. Şükran SEVİMLİ	Tıp Tarihi ve Etik	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☐	K ☒	E ☐	H ☒	E ☐	H ☒	
Prof.Dr. Sıddık KESKİN	İstatistik Uzmanı	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç.Dr. Hakkı ŞİMŞEK	Kardiyoloji	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç.Dr. Hüseyin GÜDÜCÜOĞLU	Tıbbi Mikrobiyoloji	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç.Dr.A.Faruk KIROĞLU	KBB	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Yrd.Doç.Dr. Abbas ARAS	Genel Cerrahi	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Yrd.Doç.Dr. Celaleddin SOYALP	Anesteziyoloji ve Reanimasyon	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Yrd.Doç.Dr. Numan ÇİM	Kadın Hastalıkları ve Doğum	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Yrd.Doç.Dr. Ramazan ÜSTÜN	Fizyoloji	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Yrd.Doç.Dr. Ersoy ÖKSÜZ	Farmakoloji Uzmanı	Yüzüncü Yıl Üniversitesi Tıp Fakültesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Lütfü POLAT	Eczacı	Van Polat Eczanesi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Nazlı AKTAŞ	Avukat	Yüzüncü Yıl Üniversitesi Hukuk Müşavirliği	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Özge Burak DEĞER	Sağlık Mesleği Mensubu Olmayan Üye	Van Sanayici ve İş Kadınları Derneği	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Adnan SELÇUK	Sağlık Mesleği Mensubu Olmayan Üye	Van İş Geliştirme Merkezi	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	

Sayfa 2

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ATTACHMENT 2. Plagiarism Report

YÜZÜNCÜ YIL ÜNİVERSİTESİ
SAĞLIK BİLİMLERİ ENSTİTÜSÜ
LİSANSÜSTÜ TEZ ORİJİNALLİK RAPORU

Tarih: 29/01/2018

Tez Başlığı / Konusu:
"INVESTIGATION OF BLASTOCYSTIS SP. FREQUENCY IN IMMUNOCOMPRAMISED PATIENTS"
Yukarıda başlığı/konusu belirlenen tez çalışmamın Kapak sayfası, Giriş, Ana bölümler ve Sonuç bölümlerinden oluşan toplam 32 sayfalık kısmına ilişkin, 29/01/2018 tarihinde şahsım/tez danışmanım tarafından Turnitin intihal tespit programından aşağıda belirtilen filtreleme uygulanarak alınmış olan orijinallik raporuna göre, tezimin benzerlik oranı %17 (Onyedi) dir.
Uygulanan filtreler aşağıda verilmiştir:
- Kabul ve onay sayfası hariç,
- Teşekkür hariç,
- İçindekiler hariç,
- Simge ve kısaltmalar hariç,
- Gereç ve yöntemler hariç,
- Kaynakça hariç,
- Alıntılar hariç,
-Tezden çıkan yayınlar hariç,
- 7 kelimeden daha az örtüşme içeren metin kısımları hariç (Limit match size to 7 words)

Yüzüncü Yıl Üniversitesi Lisansüstü Tez Orijinallik Raporu Alınması ve Kullanılmasına İlişkin Yönergeyi inceledim ve bu yönergede belirtilen azami benzerlik oranlarına göre tez çalışmamın herhangi bir intihal içermediğini; aksinin tespit edileceği muhtemel durumda doğabilecek her türlü hukuki sorumluluğu kabul ettiğimi ve yukarıda vermiş olduğum bilgilerin doğru olduğunu beyan ederim.

Gereğini bilgilerinize arz ederim.

Tarih ve İmza

Adı Soyadı: Akram Ahmed ISMAEL
Öğrenci No:
Anabilim Dalı: Parazitoloji
Programı: Parazitoloji
Statüsü:Y.Lisans☐ Doktora☐

DANIŞMAN ONAYI
UYGUNDUR

Prof. Dr. Zeynep TAŞ CENGİZ

ENSTİTÜ ONAYI
UYGUNDUR