ORIGINAL ARTICLE

THE CONTRIBUTION OF INTESTINAL PROTOZOA TO DIARRHOEA IN CANCER PATIENTS UNDERGOING CHEMOTHERAPY AT NATIONAL HOSPITAL ABUJA

Hannatu U. Ayuba[1], Festus Igbinoba[1], Philip Nwajiobi-Princewill[2], Sunday A. Adewuyi[3], Abbas A. Abdus-Salam[4], Rasaaq A. Oyesegun[1], Simeon C. Aruah[1], Samuel Sonibare[2], Khadijah Abdulraheem[2], Tobechi Akujiobi[2], Omonyeme Oboh[2], Abdulhamid Shehu[1], Dalhat Umar[1], Amina Dansani[1], Philip Ayom[1], Umar Aminu,[1] Kenneth Enwerem[5], Nura Shuaib[1], Fatima I Uba[1]

1. Radiotherapy and Oncology Department, National Hospital Abuja, Nigeria.
2. Medical Microbiology Department, National Hospital Abuja, Nigeria.
3. Department of Radiation and Clinical Oncology, Ahmadu Bello University Teaching Hospital Zaria, Nigeria.
4. College of Medicine, University of Ibadan, Nigeria.
5. Institute of Human Virology, Abuja, Nigeria.

Corresponding Author:
Dr Ayuba, Hannatu Usman, Radiotherapy and Oncology Department, National Hospital Abuja, Nigeria, hannatuayuba@gmail.com, +2348097046624

Citation: Ayuba HU, Igbinoba F, Nwajiobi-Princewell P, Adewuyi SA, Abdus-Salam AA, Oyesegun RA, *et al.* The Contribution of Intestinal Protozoa to Diarrhea in Cancer Patients Undergoing Chemotherapy at National Hospital Abuja. *Niger J Oncol* 2025;1(2): 201-207

ABSTRACT

Background: Diarrhoea is one of the most critical health problems worldwide. In addition, vital symptom burden in cancer patients undergoing chemotherapy, which can worsen the disease condition with poor outcomes in the presence of intestinal protozoa infestations. The study assessed the contribution of intestinal protozoa to diarrhoea in breast cancer patients undergoing chemotherapy at National Hospital Abuja. The increasing cancer burden in low and middle-income countries LMICs with emerging intestinal protozoa of public health significance makes it essential to screen such high-risk populations.

Methods: This study was an observational, case-control study of breast cancer patients undergoing chemotherapy at the Radiotherapy and Oncology Department of the National Hospital Abuja. Stool samples of breast cancer patients undergoing chemotherapy were analysed. Clinical and demographic data, along with laboratory results of the stool assays of the cases and control groups, were explored.

Results: Prevalence of intestinal protozoa in patients with diarrhoea was 24(47.1%). Twenty (39.2%) of the patients diagnosed with intestinal protozoa had complicated diarrhoea as compared with 18 (35.2%) without intestinal protozoa with complicated diarrhoea.

Conclusion: *Cryptosporidium*, *Entaemoeba coli* and *Entamoeba histolytica* were isolated and found to also contribute to diarrhoea in our breast cancer patients on chemotherapy.

Keywords: Diarrhoea, Complicated diarrhoea, Infective diarrhoea, Intestinal protozoa, Chemotherapy, *Entamoeba* spp., *Blastocystis* spp., Cryptosporidiosis, Giardiasis

INTRODUCTION

Diarrhoea is one of the most critical health problems worldwide. It is an important symptom burden in cancer patients undergoing chemotherapy, which can worsen the disease condition with poor outcomes when complicated with intestinal protozoan infestations. Majority of our patients present with complicated diarrhoea, which lead to post-chemotherapy complications and death.[1,2] Globally, there are studies on prevalence in haematological cancers and few in solid tumours.[1,3–6] The literature has rich documentation of the prevalence of intestinal protozoa parasites in diarrhoeic cancer patients. This prevalence ranges from 16% by Zdziarska r et al. in Poland, 28% by Guarner et al. in Mexico, 43.1% by Izadi et al. in Iran, 13% by Tasova et al. in Turkey, 85.5% by Abdel-mageid et al. in Egypt, 17.7% by Ayman El Badry et al. in Egypt, 17% by Sitotaw et al. in Ethiopia.[3, 7–11] There is dearth of data on the prevalence and its contribution to diarrhoea in this high-risk population locally. This challenge of intestinal protozoan infestations and complicated diarrhoea, particularly in the cancer patient on chemotherapy in the tropics, is more likely to experience an exacerbation of post-chemotherapy sequelae, debility, morbidity and even mortality when not well managed. Some research and data have been documented on causative intestinal protozoa in some high-risk groups in Nigeria, but no reported data from Nigerian cancer patients.

The study assessed the prevalence of diarrhoea associated of intestinal protozoa among breast cancer patients receiving chemotherapy in National Hospital Abuja; ascertained the types of protozoan parasites responsible for diarrhoea and the association between intestinal protozoa and complicated diarrhoea among breast cancer patients undergoing chemotherapy at National Hospital Abuja. The increasing cancer burden in low and middle-income countries LMICs with emerging intestinal protozoa of public health significance makes it essential to screen such high-risk populations.

MATERIALS AND METHODS

This study was an observational, prospective, case-control study with ethical approval number NHA/EC/011/2023. Multistage sampling technique was employed with consecutive sampling after random selection of the first participant. Sample size was calculated using the modified Fischer's formula for case control studies. Prevalence in cases from Esthegamati et al 25.9%, controls from Zdiardska et al 6%, each with attrition 10%, (alpha level 1.96, and power 80%) gave 54 for each group, at a 1:1 ratio for cases and controls, totaled at 108, approximated to 110.

Participants chosen met the inclusion criteria and exclusion criteria, they were educated with educative flyers on intestinal protozoa and definition of diarrhoea by the principal investigator and trained research assistant. They consented and signed the consent forms and were educated on stool collection methods. The participants were stratified into the diarrhoeic D and non-diarrhoeic ND groups, matched by age and gender.

Three stool samples were collected (one rectal swab with Cary Blair medium, two bulk stools in universal sample containers over 48-72hrs). Stool samples underwent macroscopic and microscopic examination with the Kato katz, wet mount, Lugol's iodine-stained smears, concentration method using mini parasep SF tubes sediment smeared on slides stained with

iodine, stool smears under cold modified Ziehl Nelson staining.

Results of these tests were retrieved; data on grading of diarrhoea, complicated and uncomplicated diarrhoea were input into the REDCAP website on the research profile. Data was cleaned, exported, SPSS format retrieved and analysed in SPSS version 28. Frequency tables, mean, standard deviation SD for continuous variables; chi square (X^2), bivariate, multivariate logistic regression of multiple variables for categorical variables: Statistical significance was set at P value <0.05

RESULTS

A total of 110 participants who met the inclusion criteria which were histopathologically confirmed breast cancer patients undergoing chemotherapy were recruited into the study groups D 51 (56.4%) ND/ Control 59 (53.6%) females 99.1%, males 1%, mean age 50.2yrs SD 10.9, postgraduate 39.1%, Married 69.1%, Self-reliant 35.5%, IHC luminal A- 39.1%, overall prevalence of intestinal protozoan parasites was 38 (34.5%).

Table 1. Prevalence of Intestinal Protozoan Parasites Amongst Breast Cancer Patients with or without diarrhoea (Objective 1)

Indication	Overall (N)	Intestinal protozoa Yes N (%)	No N (%)	χ^2	*p value*
Diarrhoea	51	24 (47.1)	27 (52.9)		
No diarrhoea	59	14 (23.7)	45 (76.3)		
Total	110	38 (34.5)	72 (65.5)	6.568	0.012

Values are presented as n (%) p-value= <0.05

About one-third of participants were diagnosed with intestinal protozoa. The overall prevalence of intestinal parasite in the population was 38(34.5%). (Answer to Objective 1) The prevalence of intestinal protozoan parasites seen in the breast cancer patients was significantly higher among patients with diarrhoea D 24(47.1%) compared to 14(23.7%) (p=0.012) in the patients without diarrhoea ND.

Table 2. Species of Intestinal Protozoan Parasites seen amongst Breast Cancer Patients on chemotherapy with positive intestinal protozoa result (Objective 2)

Parasite	Overall (*n*=38)	Diarrhoea (*n*=24)	No diarrhoea (*n*=14)	U	*p*
E. coli only	12 (31.6)	5 (20.8)	7 (50.0)	109.500	0.051
Cryptosporidium only	20 (52.6)	14 (58.3)	6 (42.9)		
E. coli & *E. histolytica*	3 (7.9)	2 (8.3)	1 (7.1)		
E. coli, E. histolytica & *Cryptosporidium*	1 (2.6)	1 (4.3)	0 (0.0)		
E. coli & *Cryptosporidium*	2 (5.3)	2 (8.3)	0 (0.0)		

The parasites and their combinations in Group D vs Group ND were observed as follows: Overall prevalence of *Entamoeba coli* only was 12(31.6%) with that in the D group 5(20.8%) compared to 7(50.0) in the ND group. Overall prevalence of *Cryptosporidium* only was 20(52.6%) with that in

D group was 14(58.3%) vs ND 6 (42.9). Overall prevalence of *Entamoeba coli* and *Entamoeba histolytica* 3(7.9%) with that in the D 2(8.3) vs 1(7.1%) in the ND group. Overall prevalence of *Entamoeba coli* and *Entamoeba histolytica* & *Cryptosporidium* is 1(2.6%) while that in D group 1(4.2%) vs 0(0%) in the ND group 1(4.2%). Overall prevalence of *Entamoeba coli* and *Cryptosporidium* is 2 (5.3%) with that in the D group 2 (8.3%) vs 0 (0%) in the ND group (P-value - 0.051).

Table 3: Association between intestinal protozoa species and complicated diarrhoea in breast cancer patients receiving chemotherapy (Objective 3)

Type of diarrhoea	Overall (*n*=24)	*E. coli* only (*n*=5)	*Cryptosporidium* only (*n*=14)	*E. coli* & *E. histolytica* (*n*=2)	*E. coli, E. histolytica* & *Cryptosporidium* (*n*=1)	*E. coli* & *Cryptosporidium* (*n*=2)	χ^2 *df =4*	*p*
Complicated	20 (83.3)	4 (80.0)	11 (78.6)	2 (100.0)	1 (100.0)	2 (100.0)	16.500	0.002
Uncomplicated	4 (16.7)	1 (20.0)	3 (21.4)	0 (0.0)	0 (0.0)	0 (0.0)	8.500	0.075

df- degree of freedom

Further subgroup analysis revealed 11(78.6%) amongst *Cryptosporidum* only group were associated with complicated diarrhoea as compared to 3(21.4%) with uncomplicated diarrhoea. While 4(80%) *Entamoeba coli* only group was associated with complicated diarrhoea compared with 1(20%) with uncomplicated diarrhoea. While 2(100%) amongst *Entamoeba coli* and *Entamoeba histolytica* group were associated with complicated diarrhoea, none with uncomplicated diarrhoea. More so, 1(100%) of the *Entamoeba coli, Entamoeba histolytica* and *Cryptosporidium* group were associated with complicated, none with uncomplicated diarrhoea. While 2(100%) of the *Entamoeba coli* and *Cryptosporidum* group was associated with complicated diarrhoea, none with uncomplicated diarrhoea.

The χ^2 is 16.5 for the complicated diarrhoea vs the protozoa parasites group. P-value is 0.002

DISCUSSION

The prevalence of intestinal protozoa among respondents with diarrhoea from this study showing bivariate analysis with p-value of 0.4 was 17(38.6%) while those without diarrhoea was 20 (30.3%). This is similar to findings by Ayman El-Badry et al, Schimdt-Hieber et al and Zdziarska *et al*.[7, 12, 13]

The prevalence of intestinal protozoa among respondents with diarrhoea from this study showing bivariate analysis with p-value of 0.4 was 17 (38.6%) while those without diarrhoea was 20 (30.3%).This prevalence is similar to studies with 16% by Aleksandar et al. in Poland, 28% by Guarner et al. in Mexico, 43.1% by Izadi et al. in Iran, 13% by Tasova et al. in Turkey, 85.5% by Abdel-mageid et al. in Egypt, 17.7% by Ayman El-Badry et al. in Egypt, 17% by Sitotaw et al. in Ethiopia.[3,9–12,14] The study revealed the population of patients with diarrhoea was 51(46.4%)

complicated diarrhoea which is defined as Diarrhoea grade 1 and 2 with complicating symptoms like abdominal cramps, vomiting, fever, blood in stool, severe weakness, shock, severe dehydration etc. and diarrhoea grades 3 and 4 were found to be 38 (74.5%).While those with uncomplicated diarrhoea comprised 13(25.5%). Multivariate logistic regression revealed that among this population of 51 patients (46.4%) that had diarrhoea, now viewed as a composite of 100%, 24 representing 47.1% of the respondents had intestinal parasites. However, 39.2% of the patients with complicated diarrhoea were diagnosed with intestinal protozoa as compared with 35.2% with complicated diarrhoea without intestinal protozoa. The odds of having complicated diarrhoea were 1.7 times more among the subjects with intestinal protozoa although the differences in the distributions were not statistically significant p- value 0.149.

CONCLUSION

The study revealed that intestinal protozoan parasites contributed significantly to diarrhoea and complicated diarrhoea amongst breast cancer patients than in those without diarrhoea.

The isolated intestinal protozoa which include *Cryptosporidium, Entaemoeba coli* and *Entamoeba histolytica contributed* significantly to diarrhoea in our breast cancer patients on chemotherapy with diarrhoea

RECOMMENDATIONS

Pre- chemotherapy screening of intestinal protozoa and other parasites, using our locally available parasitology methods and appropriate chemoprophylaxis given before the commencement of chemotherapy or these stool tests carried out in patients with persistent or complicated diarrhoea presenting at the clinic or emergency department by the oncologist.

This information should be disseminated to other healthcare workers in the multidisciplinary team to raise awareness of the need for stool tests and anti-parasitic medication to be given when such breast cancer patients on chemotherapy, or those with prior history of radiotherapy present with complicated diarrhoea symptoms. Now, the healthcare worker with a high index of suspicion will manage more appropriately.

There should be more research using wider sample size with multi-centers with more categorized, more homogenous systemic chemotherapy agents in the study with molecular studies involved for increased sensitivity and isolation of fastidious organisms.

STRENGTHS AND LIMITATIONS OF STUDY

The strength of this study is that it has raised awareness about these parasites and the symptoms they cause in our patients. It has strengthened the prescription of stool microscopy culture and sensitivity MCS in our practice among me and colleagues. It has also added to the wealth of knowledge in informing us about the prevalence of such parasites in our patients in this environment.

Limitations include the limited sample size, study carried out in one center, so the results cannot be generalized for the whole Nigerian population. Financial constraint, which limited the procuring of laboratory consumables and molecular tests not allowing for a bigger sample size. The study is not a longitudinal study as following up these patients is vital to

see the trends in outcomes of treatment and survival.

REFERENCES

1. M.M Sanad; F. A Thagfan, A. Al Hammad, E.M Olayan, A. Almogren. Opportunistic Coccidian Parasites among Saudi Cancer Patients Presenting with Diarrhea: Prevalence and Immune Status [Internet]. Cited: https://scialert.net/fulltext/?doi=jp.2014.55.63
2. Stein A, Voigt W, Jordan K. Chemotherapy-induced diarrhea: pathophysiology, frequency and guideline-based management. Ther Adv Med Oncol. 2010; 2(1):51. Cited: /pmc/articles/PMC3126005/
3. Sitotaw E, Sitotaw A, Aleka Y, Lemma M. Prevalence of Intestinal Helminths among Cancer Patients Who Are under Chemotherapy at the University of Gondar Comprehensive Specialized Hospital Oncology Clinic, Northwest Ethiopia. J Cancer Epidemiol. 2022:4484183.
4. Al-Qobati SA, Al-Maktari MT, Al-Zoa AMB, Derhim M. Intestinal parasitosis among Yemeni patients with cancer, Sana'a, Yemen. J Egypt Soc Parasitol. 2012; 42(3):727–34. Cited: https://pubmed.ncbi.nlm.nih.gov/23469646/
5. Al-Yousofi A, Aabarhara Y. "Prevalence of Intestinal Parasites among Immunocompromised Patients, Children, and Adults in Sana'a, Yemen",0. J Trop Med. 2022;42(3):727-734.
6. Banihashemi SM, Soleymani E, Abdizadeh R, Motavalli Haghi M, Khalili B. Intestinal Protozoan Infections in Cancer Patients Undergoing Chemotherapy in Shahrekord the Central Southwest of Iran in 2018. Int J Epidemiol Res. 2020 Nov 1; 7(4):144–51. Cited: http://ijer.skums.ac.ir/article_44726.html
7. Łanocha A, Łanocha-Arendarczyk N, Wilczyńska D, Zdziarska B, & Kosik-Bogacka D. Protozoan Intestinal Parasitic Infection in Patients with Hematological Malignancies. J Clin Med. 2022; 11(10). Cited: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9146298/
8. Izadi S, Ghayour-Najafabadi Z, Yavari M, Mohaghegh MA, Wannigama DL, Moslemzadeh HR, et al. Intestinal Parasites Associated with Opportunistic Coccidial Infections Among Immunocompromised Individuals in Central Iran: A Cross-Sectional Study. Arch Clin Infect Dis 2019 142. 2019; 14(2):79701. Cited: https://brieflands.com/articles/archcid-79701.html
9. El-Nemr; AAAMWAEGHI, A. EHA. Prevalence of Intestinal Parasites in Cancer Therapy Recipients with Concurrent Diarrhea. Int J Trop Dis Heal. 2016; 15(1):1–7. Cited: www.sciencedomain.org
10. J Guarner, R Villasenor-Flores, G Sanchez-Memoranda, T Mailed-Nava. Frequency of intestinal parasites in adult cancer patients in Mexico. Arch Med Res. 1997;28(2):219-222
11. Taşova Y, Şahin B, Koltaş S, Paydaş S. Clinical significance and frequency of Blastocystis hominis in Turkish patients with hematological malignancy. Acta Med Okayama. 2000; 54(3):133–6. Cited:

https://pubmed.ncbi.nlm.nih.gov/10925738/

12. El-Badry AA, El Sayed SS, Hussein RR, Said YM, Al-Antably AS, Hassan MA. Intestinal parasitism in pediatric oncology children receiving chemotherapy: unexpected low prevalence. Heliyon. 2019;5(8):e02228.
13. Schmidt-Hieber M, Bierwirth J, Buchheidt D, Cornely OA, Hentrich M, Maschmeyer G, et al. Diagnosis and management of gastrointestinal complications in adult cancer patients: 2017 updated evidence-based guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Medical Oncology (DGHO). Ann Hematol. 2017; 97(1):31–49. Cited: https://link.springer.com/article/10.1007/s00277-017-3183-7
14. Radojevic MZ, Tomasevic A, Karapandzic VP, Milosavljevic N, Jankovic S, Folic M. Acute chemoradiotherapy toxicity in cervical cancer patients. Open Med. 2020; 15(1):822–32.