Cryptosporidiosis in Renal Transplant Recipients: Uncovering Risk Factors, Treatment Strategies, and the Role of Food Handlers in Transmission

Abstract

Background: *Cryptosporidium* is a common but understudied cause of diarrhea in solid organ transplant recipients. We explored its prevalence, risk factors, treatment strategies, and transmission through food handlers in renal transplant recipients (RTRs). **Materials and Methods:** A retrospective analysis was conducted over a year at a tertiary hospital, focusing on RTRs with diarrhea. Diarrhea was bifurcated into *Cryptosporidium*-related and non-*Cryptosporidium* diarrhea for comparative analysis. **Results:** Among 60 RTRs with diarrhea, 18 (30%) had *Cryptosporidium* infection. The *Cryptosporidium* group (66.7%, p=0.04) saw more frequent induction with anti-thymocyte globulin (ATG). Within 6 months of induction therapy or rejection treatment with pulse steroids, 72% of cases occurred. Higher rates of Cryptosporidiosis were observed with non-vegetarian diets (83.3%, p=0.01), lower education levels (p=0.01), and consumption of unboiled water (72.2%, p=0.15). Hospitalization was higher in the *Cryptosporidium* group (88.9%, p=0.01). Co-infections occurred in 27.8%, with extra-intestinal manifestations in 83%. Modification in immunosuppressive therapy was required in 66.7% (p<0.001). Relapse occurred in 12% of patients; all had infected food handlers. Graft complications were frequent in the *Cryptosporidium* group (38.9%, p=0.002). Food handlers had higher infection rates in the *Cryptosporidium* positive group (55.5% vs. 4.8%, p<0.01, OR=25). **Conclusion:** *Cryptosporidium* infection in RTRs is linked to immunosuppression, dietary habits, and poor hygiene among food handlers. Effective management requires education, improved hygiene, and immunosuppressive adjustments.

Keywords: *Cryptosporidium infection, Food handlers, Post transplant diarrhea*

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Introduction

Diarrhea is a common yet underestimated complication of kidney transplantation, significantly impacting the quality of life and leading to serious complications such as dehydration, malabsorption, and increased risk of graft loss. Renal transplant recipients (RTRs) are particularly vulnerable to various diarrhea-causing organisms, including *Clostridium difficile,* Cytomegalovirus, Norovirus, and *Cryptosporidium.* This article focuses on Cryptosporidiosis, a parasitic infection that poses a significant health risk to immunocompromised individuals. Immunosuppressive therapy, while essential for preventing organ rejection, weakens the immune system, leaving RTRs more susceptible to infections like *Cryptosporidium*, which can cause severe illness and in some cases, be life-threatening.[1] Studies have shown a 10-30% prevalence of *Cryptosporidium* infection in RTRs with chronic diarrhea.[1,2] The disease severity is further compounded by its potential to cause acute graft dysfunction and prolong hospitalizations. Research indicates that 18-83% of RTRs with cryptosporidiosis experience renal graft dysfunction, which can lead to graft loss in severe cases.[3,4] While the prevalence of *Cryptosporidium* infections varies by region and population, it is significant among individuals with compromised immunity.[5] Several factors, such as the type of immunosuppressive regimen, food handling practices, and hygiene, can influence infection risk and severity.[1,6] Medication like nitazoxanide and fluoroquinolones is available, but the optimal management strategy for *Cryptosporidium* in RTRs remains unclear.[6] This study aims to assess the prevalence, risk factors, and treatment options for cryptosporidiosis among RTRs, with a particular focus on the role of food handlers in transmission.

Materials and Methods

This retrospective study was conducted at Osmania General hospital in South India from January 2022 to January 2023. We identified RTRs with diarrhea who required evaluation and hospitalization. Inclusion criteria encompassed all RTRs presenting to the hospital with diarrhea (both OPD and IPD patients). All underwent stool analysis for *Cryptosporidium,* along with the food-handlers, routinely. This protocol ensured that both patient and food handler data were systematically documented in the medical records. *Cryptosporidium* was detected through stool microscopy using acid-fast staining and confirmed with fluorescent microscopy. Data were extracted from medical records using a standardized data collection form. Patient's consent was taken stating that all data would be anonymized. Ethics committee approval was not required as it was retrospective data collection.

Information collected included patient demographics, including age, sex, education status, dietary habits (vegetarian or non-vegetarian), source of drinking water, and native kidney disease. Transplant data, including type of transplant (live or deceased donor), type of induction therapy, maintenance immunosuppressive regimen, history of recent rejection episodes (within the last 6 months) treated with either anti-thymocyte globulin (ATG) or pulse steroids, and the time gap between Cryptosporidiosis and induction or recent rejection treatment, were collected. Clinical details including extra-gastrointestinal presentations, co-infections (e.g., Cytomegalovirus-CMV, Parvovirus B19, Tuberculosis-TB, *Salmonella*), hospitalization requirement, graft dysfunction, treatment regimens (monotherapy with nitazoxanide or combination therapy with nitazoxanide plus macrolides &/ fluoroquinolones), modifications in immunosuppression, and treatment duration were noted. Food handlers of all patients were subjected to stool microscopy with acid-fast staining and fluorescent microscopy. Treatment protocols and modifications in immunosuppression have been elaborated in Figure 1. Treatment response was assessed by clinical symptom resolution and/or oocyte clearance, as determined by twice-repeat microscopy. Remission was defined as the resolution of symptoms combined with oocyte clearance. If oocyte clearance was achieved but symptoms persisted, patients were evaluated for other causes, such as CMV, *Clostridium*, or malabsorption syndrome. Tacrolimus levels were measured during diarrheal episodes in case of renal dysfunction or features suggestive of tacrolimus toxicity. Doses were adjusted according to their levels. Follow-up was conducted to monitor for relapse in patients who achieved remission, evaluate recovery in those with graft dysfunction, and adjust immunosuppressive medications once remission was attained. Food handlers were referred to family members for living with and preparing meals for RTRs throughout their illness. Due to close contact with the patients, stool samples from them were assessed for potential transmission. When *Cryptosporidium* was detected in the food handlers, they were educated on proper hygiene practices, but no treatment was administered as all remained asymptomatic. The study used comprehensive electronic medical records with minimal missing data, primarily related to follow-up information for patients who

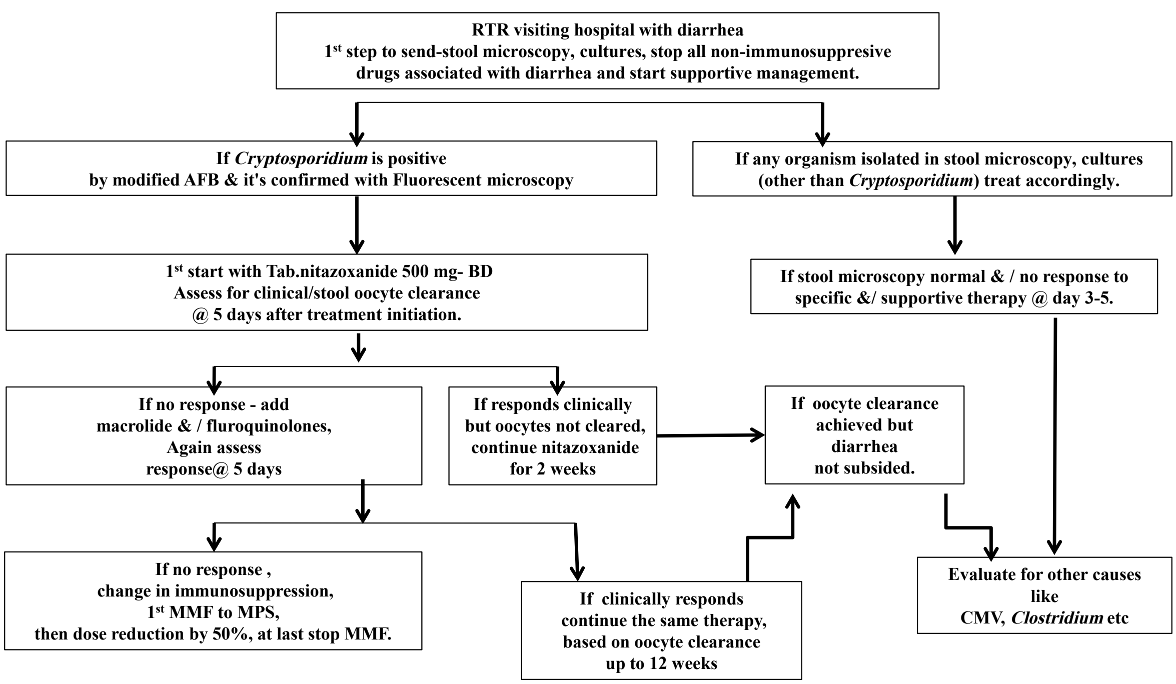

Figure 1: Management protocols followed in RTRs visiting hospital with diarrhea. RTR: Renal transplant recipient, CMV: Cytomegalovirus, MMF: Mycophenolate mofetil, MPS: Mycophenolate mofetil sodium, AFB: Acd fast bacilli, BD: Twice in a day.

passed away during the study. These cases were excluded from follow-up analyses to ensure they did not affect the overall findings.

Statistical analysis

The study utilized descriptive and inferential statistics to analyze the prevalence and factors associated with *Cryptosporidium* infection in RTRs. Descriptive statistics summarized demographic and clinical characteristics; categorical variables were presented as frequencies and percentages, while continuous variables were reported as mean and standard deviation. For inferential analysis, the Chi-square test assessed associations between categorical variables (e.g., education level, diet, water source, and infection status), while the independent sample t-test compared means between *Cryptosporidium*-positive and negative groups. For paired data, McNemar's test was applied. Statistical significance was set at $p<0.05$. All analyses were conducted using jamovi 2.5.3 to ensure accuracy and rigor in identifying patterns and associations in infection prevalence and risk factors among RTRs.

Results

A total of 96 RTRs were followed up, with 60 experiencing diarrhea. Among these, 18 (30%) were diagnosed with *Cryptosporidium* infection. The mean age of the participants was 36.7 ± 7.9 years; a majority were male (66.7%). The main causes of kidney disease were chronic glomerulonephritis (CGN) (n=9, 50%), chronic interstitial nephritis (CIN) (n=5, 27.8%), CKD-unknown (n=3, 16.7%), and other causes (n=1, 5.6%). Regarding educational status, 22.2% had no formal education, 22.2% had primary schooling (10th grade), 33.3% had secondary/ higher secondary education (12th grade), and 22.3% were graduates [Table 1]. Around 83.3% of participants were non-vegetarians. Approximately 83.3% used municipal (chlorinated) water, while 27.8% relied on groundwater (boiled). Thirteen (72.2%) and five (27.8%) transplants were from living and deceased donors, respectively. Induction therapy with ATG was administered to 66.7% of participants, while 33.3% did not receive it. All patients (100%) were maintained on triple immunosuppression therapy with mycophenolate mofetil (MMF), tacrolimus, and prednisolone. Infections developed in 72.2% of participants, either within 6 months post-transplant or following treatment for rejection with ATG/pulse steroids. The remaining 27.8% were >6 months post-transplant at infection onset. Hospitalization was required for 88.9% of patients diagnosed with Cryptosporidiosis. Co-infections were observed in 27.8% of patients and included Parvovirus B19 (5.6%), tuberculous meningitis (5.6%), CMV (11.1%), and sporotrichosis (5.6%). The most common extra-gastrointestinal symptom reported was weight loss, affecting 44.7% of patients [Figure 2]. Graft dysfunction occurred in 38.9% of cases, most commonly due to hypotension and dehydration. Among these, 86% (6/7 patients) recovered without requiring dialysis, while one (14%) died before evaluation due to co-infection with tuberculous meningitis. The treatment approaches and responses to various therapies have been listed in Figure 1 and Tables 2 and 3, respectively. Immunosuppressive modification was done to achieve the response mentioned in Figure 3. Half the patients (50%) were treated for 4 weeks, while 27.8% received treatment for 2 weeks and 22.2% for >6 weeks. Relapse was observed in 12% of the patients. Food handler testing revealed that 55.6% of patients with Cryptosporidiosis tested positive for the infection, while 44.4% tested negative. Among non-*Cryptosporidium* cases, 94.4% food handlers tested negative, indicating that transmission from food handlers primarily affected those with *Cryptosporidium* infections.

Table 1: Comparative analysis between RTRs with *Cryptosporidium*-related diarrhea vs. Non-*Cryptosporidium* diarrhea group (N = 60)

Characteristics	RTRs with diarrhea		*p*-value
	Cryptosporidium-related (n=18)	Non-*Cryptosporidium* (n=42)	
Education status			0.015
None	4 (22.2%)	0 (0.0%)	
Primary schooling	4 (22.2%)	9 (21.4%)	
Secondary schooling	6 (33.3%)	17 (40.5%)	
Graduation	4 (22.2%)	16 (38.1%)	
Diet			0.010
Non-vegetarian	15 (83.3%)	20 (47.6%)	
Vegetarian	3 (16.7%)	22 (52.4%)	
Water source			0.153
Municipal (unboiled)	13 (72.2%)	22 (52.4%)	
Ground (boiled)	5 (27.8%)	20 (47.6%)	
Induction			0.042
ATG	12 (66.7%)	16 (38.1%)	
Nil	6 (33.3%)	26 (61.9%)	
Requiring hospitalization			0.014
Yes	16 (88.9%)	16 (38.1%)	
No	2 (11.1%)	26 (61.9%)	
Co-infection			0.014
Yes	5 (27.8%)	5 (11.9%)	
No	13 (72.2%)	37 (88.1%)	
Food handler status			<0.001
Positive	10 (55.5%)	2 (4.8%)	
Negative	8 (44.4%)	40 (95.2%)	

RTRs: Renal transplant recipients, ATG: Anti thymocyte globulin.

Statistical analysis showed significant associations between *Cryptosporidium* infection and several factors. Patients without formal education had higher *Cryptosporidium* infection rates (p=0.015). Around 83.3% of *Cryptosporidium*-positive individuals reported a non-vegetarian diet, compared with 47.6% in those without

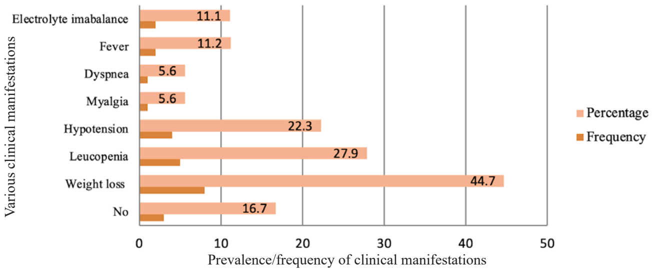

Figure 2: Extra-gastro-intestinal presentations in RTRs with cryptosporidiosis. RTR: Renal transplant recipient.

Table 2: Comparative analysis of treatment outcomes in RTRs with *Cryptosporidium*-related diarrhea vs. non-*Cryptosporidium* diarrhea group (N = 60)

Characteristics	RTRs with diarrhea		*p*-value
	Cryptosporidium-related (n=18)	Non-*Cryptosporidium* (n=42)	
Treated on OPD basis or IPD			0.014
IPD	16 (88.9%)	16 (38.1%)	
OPD	2 (11.1%)	26 (61.9%)	
Response to therapy			
Responded to initial supportive therapy	NA	37 (88.1%)	
Not responded and further evaluated for the cause	NA	5 (11.9%)	
Causes for non-response to supportive therapy/Co-infections			
CMV infection	2 (11.2%)	3 (7.1%)	
Salmonella	0 (0.0%)	1 (2.3%)	
Colitis	0 (0.0%)	1 (2.3%)	
Sporothrix	3 (5.6%)	0 (0.0%)	
TB meningitis	3 (5.6%)	0 (0.0%)	
Parvo-B19	3 (5.6%)	0 (0.0%)	
Requiring a change in immunosuppresion			<0.001
Yes	12 (66.7%)	5 (11.9%)	
No	6 (33.3%)	37 (88.1%)	
Effect on graft (renal dysfunction)			0.002
Yes	7 (38.9%)	3 (7.1%)	
No	11 (61.1%)	39 (92.9%)	
Causes of renal dysfunction			
Sepsis	1 (5.5%)	1 (2.3%)	
Hypotension	3 (16.6%)	1 (2.3%)	
Dehydration	2 (11.1%)	0 (0.0%)	
CNI-toxicity	1 (5.5%)	1 (2.3%)	

CMV: Cytomegalovirus, CNI: Calcineurin inhibitor, NA: Not applicable, IPD: In patient department, OPD: Out patient department, TB: Tuberculosis, RTR: Renal transplant recipient

Table 3: Comparative analysis of different types of therapy vs. their response in RTRs with Cryptosporidiosis (n = 18)

Therapy	Response to therapy		*p*-value
	Yes	No	
Monotherapy with nitazoxanide	5	13	0.453
Combination therapy (Nitazoxanide + Azithromycin &/ Levofloxacin)	2	11	0.003
Combination therapy + Change in immunosuppression	11	0	0.002

RTRs: Renal transplant recipients.

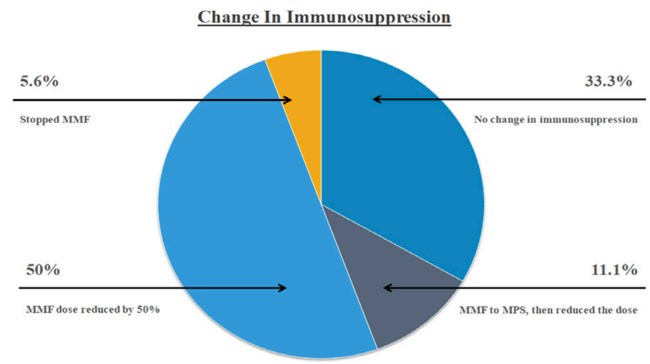

Figure 3: Immunosuppressive modification done in RTRs with Cryptosporidiosis to achieve response. MMF: Mycophenolate mofetil, MPS: Mycophenolate mofetil sodium, RTR: Renal transplant recipient

the infection (p=0.010). Induction therapy with ATG was common among those with the infection (66.7% vs. 38.1%, p=0.042). Hospitalization needs were higher in the *Cryptosporidium*-positive group, with 88.9% requiring hospital care vs. 38.1% in the non-*Cryptosporidium* group (p<0.001). Co-infections were more frequent among those with *Cryptosporidium* vs. 11.9% in the non-*Cryptosporidium* group (p=0.014). Additionally, 66.7% of *Cryptosporidium*-positive patients required changes to their immunosuppressive treatment (p<0.001), and graft-related complications were seen in 38.9% of these patients, compared with only 7.1% in the non-*Cryptosporidium* group (p=0.002). Food handling appeared to be an important factor, as 56% of food handlers tested positive for *Cryptosporidium*, compared to only 5% in the non-*Cryptosporidium* group (p<0.01, odds ratio=25). A detailed analysis has been provided in Table 1 and Table 2.

Discussion

The study on Cryptosporidiosis in RTRs offers important insights into the risks, treatments, and outcomes of this infection in immunocompromised patients. One key finding is the high Cryptosporidiosis frequency among RTRs. Age and sex distribution of patients in this study matches earlier studies.[5] The study saw a 30% prevalence of *Cryptosporidium* infection. Bhadauria *et al.*[1] state that a significant number (34/119, 28.5%) of RTRs with diarrhea may be affected, highlighting the need for routine screening in post-transplant diarrhea patients. Our study identified municipal water as the primary source in >70% of patients. This is significant because *Cryptosporidium* is often transmitted via water,[7] particularly non-boiled water. This is because boiling, not chlorination, kills the oocytes. This highlights the need for careful monitoring of water safety. About 83.3% of RTRs had a non-vegetarian diet, which can be a *Cryptosporidium* source. Chalmers *et al*.[8] also determined food-borne transmission as a concern for immunosuppressed populations. The fact that 55.6% of patients had positive food handler status reinforces the potential risk of contaminated food. This emphasizes the need for strict food safety practices. RTRs without formal education had a higher infection, likely due to limited awareness of hygiene practices and preventive measures. This aligns with research by Checkley *et al.*,[7] which emphasized that lower education levels can correlate with poorer hygiene practices, increasing the infection risk in immunocompromised populations. Induction therapy, hospitalization, and co-infections also played a significant role in *Cryptosporidium* infection status. This study found that patients on ATG induction therapy had a higher infection rate, consistent with findings by Kapel *et al.*,[9] who reported that intensive immunosuppression increases susceptibility to opportunistic infections like Cryptosporidiosis. The need for hospitalization in 88.9% of *Cryptosporidium*-infected patients further illustrates the infection's severity, as Kapel *et al*.[9] similarly observed high morbidity rates in RTRs with *Cryptosporidium*. This suggests that infections in RTRs can result in severe complications, necessitating close monitoring and prompt medical intervention. Co-infections were significant, with 27.8% of patients having other infections like Parvovirus B-19 and CMV. This aligns with findings from other studies showing the risk for multiple infections in immunocompromised patients. Research by Kotloff *et al.*[10] highlights the need for comprehensive care in RTRs, as these co-infections can worsen Cryptosporidiosis and complicate treatment.

Another important finding was the impact of Cryptosporidiosis on graft function, as shown in earlier studies,[9] which showed that Cryptosporidiosis can cause graft failure.

The treatment strategies primarily involved nitazoxanide, either alone or with azithromycin. This is consistent with existing literature. However, Cabada *et al*.[11] noted that nitazoxanide might not be effective in severely immunosuppressed individuals, necessitating the use of combination therapies. Adapting therapy to each patient's condition is crucial for better outcomes and effective infection control. Relapse occurred in 12% of the patients**;** in all of them food handlers were positive for *Cryptosporidium*, indicating the importance of repeating stool microscopy even in food handlers and educating them regarding good hygiene practices.

Our study contributes important insights into several risk factors associated with Cryptosporidiosis in RTRs. It emphasizes how dietary habits, education status, and water sources can inform targeted prevention strategies. Additionally, the impact of induction therapy as a risk factor emphasizes the need for judicious immunosuppression. The study highlights that a high index of suspicion, monitoring, and timely intervention can prevent graft dysfunction. Lastly, the high positivity rate among food handlers underscores the necessity for enhanced food safety measures to protect RTRs from potential infections.

The findings may have limited generalizability as the study was conducted at a single center with a small sample size. The retrospective design and dependence on existing records could introduce potential biases. Additionally, the study lacked molecular characterization of *Cryptosporidium* species, which may limit the depth of its conclusions. This study does not establish causality but highlights the need for further investigation into transmission dynamics.

To conclude, this study reinforces the importance of safe water and food practices, early detection of infection, and tailored treatment regimens. The study highlights the complexity of managing infections in an immunocompromised population, where the interplay between infection control and immunosuppressive therapy must be carefully managed to protect both the patient and the transplanted organ. Further research is needed to refine treatment protocols and preventive strategies, particularly in regions with limited access to clean water and robust healthcare infrastructure.

Conflicts of interest: There are no conflicts of interest.

The authors declare that no generative AI or AI-assisted tools were used in drafting, editing, or preparing this manuscript.

References

1. Bhadauria D, Goel A, Kaul A, Sharma RK, Gupta A, Ruhela V, *et al*. *Cryptosporidium* infection after renal transplantation in an endemic area. Transpl Infect Dis 2015;17:48-55.
2. Florescu DF, Sandkovsky U. Cryptosporidium infection in solid organ transplantation. World J Transplant 2016;6:460-71.
3. Krause, Irit MD; Amir, Jacob MD et al cryptosporidiosis in children following solid organ transplantation. Pediatric Infectious Disease Journal 31:p 1135-8.
4. Bandin F, Kwon T, Linas MD, Guigonis V et al Cryptosporidiosis in Pediatric renal transplantation. Pediatr Nephrol 2009;24:2245-55.
5. Cama VA, Bern C, Roberts J, Cabrera L, Sterling CR, Ortega Y, *et al*. *Cryptosporidium* species and subtypes and clinical manifestations in children, Peru. Emerg Infect Dis 2008;14: 1567-74.

6. Udgiri N, Minz M, Kashyap R, Heer M, Gupta CS, Mohandas K, *et al*. Intestinal cryptosporidiasis in living related renal transplant recipients. Transplant Proc 2004;36:2128-9.
7. Checkley W, White AC, Jaganath D, Arrowood MJ, Chalmers RM, Chen XM, *et al*. A review of the global burden, novel diagnostics, therapeutics, and vaccine targets for *Cryptosporidium*. Lancet Infect Dis 2015;15:85-94.
8. Ryan U, Hijjawi N, Xiao LFoodborne cryptosporidiosis.Int J Parasitol. 2018;48:1-12.
9. Lanternier F, Amazzough K, Favennec L, Mamzer-Bruneel MF, Abdoul H, Tourret J, *et al*. ANOFEL Cryptosporidium national network and transplant cryptosporidium study group. Cryptosporidium spp. Infection in solid organ transplantation: The nationwide "TRANSCRYPTO" study. Transplantation 2017;101:826-30.
10. Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, *et al*. Burden and aetiology of diarrhoeal disease among infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. The Lancet 2018;382:209-22
11. Cabada MM, White AC. Treatment of cryptosporidiosis: Do we know what we think we know? Curr Opin Infect Dis 2010;23: 494-9.