

## ANSWERING REVIEWERS

**Name of journal:** World Journal of Transplantation

**ESPS manuscript NO:** 24806

**Title:** *Cryptosporidium* infection in solid organ transplantation

**REVIEWER'S CODE:** 00504119

### *Comments To Authors*

the review has been written the aspects of this review are important and can be the memory to the liver transplantation team the problems about post-transplantation diarrhea

A: We Thank the reviewer for the comments.

**REVIEWER'S CODE:** 00504811

### *Comments To Authors*

This is a well written review of the epidemiology, diagnosis and management of cryptosporidium in solid organ transplant.

1. Abstract The last sentence should mention cryptosporidium. Epidemiology What is the prevalence worldwide?

A: thank you, we modified the abstract accordingly.

2. Virulence What is the incubation period.

A: we have added it to the section.

3. Some updates need to be made to the following references... remove 63 and add Pantenburg..., change ref for more recent...

A: reference 63 is an important reference and not very old (Santaolalla 2011). We added Pantenburg as well.

4. Last paragraph. Give more data about the statement saying that tacrolimus had a significantly higher risk.

A: we added more data on the study.

5. Treatment Include more information about the drugs Nitazoxanide - What is the MOA? It is only available as a suspension. Are there any precautions? Interactions? Special dosing



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in renal or hepatic impairment?

A: thanks for the suggestion. We added more information on nitazoxanide

6. Paromomycin Can you give with FK? Is there additive nephrotoxicity?

A: paromomycin does not interact with FK. any aminoglycoside that may be absorbed systemically can potentially cause nephrotoxicity but there is no data on paromomycin.

Bissuel et al. Absence of systemic absorption of oral paromomycin during long-term, high-dose

treatment for cryptosporidiosis in AIDS. Infect Dis. 1994 Sep;170(3):749-50.

7. Prevention Could food be contaminated? Should you practice safe sex? Don't swallow recreational water. Avoid anything that can be contaminated by stool. What should a person that has Cryptosporidium do to prevent infection in household members/close contacts?

A: Thanks for raising this point. We have added more details to the section and included a link to the CDC page as well.

**REVIEWER'S CODE:** 00504842

### *Comments To Authors*

Dear authors, Please find my comments in brief regarding your review paper "Cryptosporidium Infection in Solid Organ Transplantation". Infections are very common complication in solid organ transplant recipients.

1. Your manuscript is mainly focused on kidney transplant recipients. It would be interesting to know statistics, clinical manifestations, complications, and graft outcome in other organ recipients.

A: the reviewer is correct, however we just cited the known literature. We do not have data on other organs unfortunately as it has not been published.

2. Description of parthenogenesis of Cryptosporidium infection requires significant clarification. For example, it would be interesting to know what NF-KB cells are.

A: in the manuscript we refer to activated cells expressing NF-KB which in turn produce certain chemokines and may induce intestinal epithelial cell apoptosis .

3. Overall the manuscript should be reviewed/edited more carefully with deeper logical analysis of immunological events involved in the disease development. Sincerely, Reviewer.

A: thank you. We have added different paragraphs and sentences as per all the reviewers comments.



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**REVIEWER'S CODE:** 00522338

### *Comments To Authors*

This is a well written report and quite comprehensive. For it to be clinically useful, it should provide a greater summary and synthesis of the information - rather than simply list all the cases that have been reported in the literature.

1. At the current time, the tables just list the papers. I recommend that these provide summaries of the papers - how many patients were reported in kidney tx, liver tx, etc. How many patients were on what immunosuppression? This would help to better provide an estimate of prevalence and identify risk factors for such infection.

A: we agree that there should be a better understanding on risk factors and incidence or cryptosporidium. Our aim was to review the literature and we found that it consists mostly of case reports but no prospective studies or even case-control studies. As the reviewer points out, we listed the reported cases in the tables but it would be misleading for readers to try to determine prevalence and risk factors based on the available data as we do not know the denominator in most studies, so we cannot calculate prevalence or incidence. Reporting bias and underreporting are also likely as we do not know all the cases of cryptosporidium nor all have been reported.

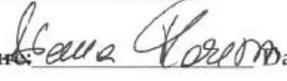
**REVIEWER'S CODE:** 00543124

### *Comments To Authors*

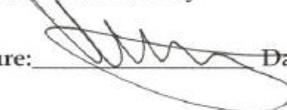
This review deals with an important issue, it is comprehensive and well written.

A: Thanks for the comments.

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Signature:  Date: 2/21/16

Name: Uriel Sandkovsky

Signature:  Date: 4/21/2016