April 30, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2663-review.doc).

**Title:** Gram – negative bacteria causing infective endocarditis – Rare cardiac complication after liver transplantation

**Author:** Susan George, Joy Varghese, Sujatha Chandrasekhar, Rajasekar Perumalla, Mettu Srinivas Reddy, Venkataraman Jayanthi, Mohamed Rela

**Name of Journal:** *World Journal of Hepatology*

**ESPS Manuscript NO:** 2663

The manuscript has been improved according to the suggestions of reviewers:

1. Revision has been made according to the suggestions of the reviewer

(1) Running title included

(2) All authors affiliation & contributions included

(3) Corresponding author’s contact detail included

(4) Abstract, Core tip & Introduction included

(5) Pubmed citation & DOI number to the references are included

2. Major and minor comments of reviewer have been answered in a separate sheet

**Reviewer’s comments**

**Major comments:**

1. India is one of the countries in the world with highest rates of ESBL in E. coli with reported rates > 50% of E. coli isolated. Therefore, ESBL in urine and blood cultures is quite common. How can the authors be sure, that the patient did not have urinary tract infection and an infection with an additional bacterial strain (VRE, Staphylococcus aureus, Streptococcus) which was also sensitive and effectively treated by Tigecyclin and missed in the cultures?

Reply: This is possible. We will agree. However, based on evidence of available culture reports before and after therapy, we are reporting this case.

2. Did the bacterial strains isolated from the blood and urine show the same antibiogram?

Reply: Yes. It showed the same antibiogram.

3. How many blood cultures were preserved before antibiotics were started?

Reply: Three blood cultures

4. Why did the authors treat endocarditis with Meropenem and Tigecyclin and not another regime? Aminoglycosides, as Amikacin are widely used for treatment of endocarditis? Please discuss.

Reply: Both the blood & urine culture sensitive report showed that organism was sensitive to the Meropenem, Tigecyclin and Aminoglycoside. As the patient had renal dysfunction (serum creatinine was 1.8) as well as he was already taking immunosuppressive drug (tacrolimus)which is also a nephrotoxic agent, we did not use aminoglycoside.

5. How did the patient acquire E. coli in the blood other than form the urinary tract?

Reply: No other evident focus of infection.

6. Do the authors speculate that urinary tract infection and concomitant bacteremia lead to population of the valve?

Reply: Yes.

7. Did the patient undergo any medical or dental treatment which may cause bacteremia between transplantation and presentation with endocarditis?

Reply: No.

8. The authors stated: “In conclusion, a high index of suspicion especially new onset of auscultation findings at cardiac valve area and initiating empirical broad spectrum antibiotics at the earliest before getting culture sensitivity report in LT recipient is important”. Early antibiotic treatment for severe infections in immunosuppressed patients is an obvious rule. Therefore, the conclusion is poor. However, obtaining of several cultures is highly recommended, and should be one of the conclusions of the present report as ESBL should be hit by the antibiotic regimen!

Reply: Agreed. This has been included in the conclusion.

9. As ESBL E. coli is postulated for empiric antibiotic treatment also KPCs should be mentioned. What kind of antibiotic regimen do the authors recommend for empiric treatment if KPC are also in the game?

Reply: If KPC or NDM were the case, then colistin with a carbapenem would be best.

**Minor comment:**

1. Pictures of the populated valves and antibiograms could be added.

Reply: As the ECHO pictures quality was not better, it has not been added.

2. Did the patient have other signs of endocarditis (septic embolism, etc.)?

Reply: No

3. What about the red blood cells in the urine? Did they present as dysmorphic erythrocytes in the sediment fitting to glomerulonpehritis?

Reply: Yes.

Thank you again for publishing our manuscript in the *World Journal of Hepatology.*

Sincerely yours,

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