



To the editors of
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**“Severe infection with multi-drug resistant Salmonella choleraesuis
in a young patient with primary sclerosing cholangitis”**

Dear Mr. Ma,

Dear editors of *WJG*,

Thank you very much for your concise and thoughtful review of the above mentioned manuscript. We looked through your advice carefully, and want to thank you for the highlighted points that helped us working out key arguments of the manuscript. In the following, you will find our adjustments based on your reviews.

Comment #1: The authors reported a case of cholangitis caused by multi-drug resistant salmonella spp. In patients with obstructive pathology of biliary tract, bacterial cholangitis is a common condition. I think that the primary purpose of this article should be to highlight of cholangitis caused by multi-drug resistant salmonella infection in sclerosing cholangitis. So it would be more appropriate the title “multi-drug resistant salmonella infection in primary sclerosing cholangitis or ESBL and MDR salmonella spp in primary sclerosing cholangitis. In abstract section the sentence- “ESBL resistance of Salmonella enterica spp. should be considered in patients with obstructive biliary tract pathology and a travel history in endemic countries.” would be more appropriate. And this topic should be discussed in discussion section.

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Reply #1:

Yellow mark - Our initial purpose was to draw the readers' attention by giving the case an unspecific heading. Since MDR is a key issue in the given setting, we followed your suggestion and amended the title of the manuscript: Severe infection with multidrug-resistant *Salmonella choleraesuis* in a young patient with primary sclerosing cholangitis (lines 4-5, 87-88)

Green mark - Amended: ESBL resistance of *Salmonella enterica* spp. should be considered in patients with obstructive biliary tract pathology and travel history in endemic countries (lines 67-69).

Blue mark - We feel that in the introduction section, strong emphasis has been made on the susceptibility of patients with primary sclerosing cholangitis for invasive salmonellosis. We added another causative connection to the discussion section, arguing that predisposing biliary diseases are a stepstone towards development of MDR Salmonellosis, and added two more references: While antibiotic treatment is not recommended in asymptomatic shedders of *Salmonella* spp. or in uncomplicated gastroenteritis^{[15][16]}, MDR resistant *Salmonella* is likely to have a critical impact in patients with obstructive biliary tract pathology and altered bile constitution. Since global burden of MDR *Salmonella* spp. keeps rising, this alarming development is reflected by our case report on travel-associated salmonellosis with serotype Choleraesuis expressing ESBL and additional resistance to fluoroquinolones (lines 164-170).

Comment #2: The authors reported a case in which the patient suffered from watery diarrhea, cramps in the lower abdomen and fever for six days due to an infection by Salmonella spp. supposedly acquired during a trip to Thailand. The rising global burden of MDR non-typhoidal Salmonella spp. was mentioned in the manuscript discussion and attributed to increasing tourism to South-East Asia. Considering the increase of the endemic diseases from developing

countries in Europe, *it would be interesting to present the data regarding these registered cases in Germany and/or Europe. It's also important to know if the diagnosis and treatment were similar.*

Although this was an isolated case, it can improve the knowledge about tropical disease routes in Europe and share protocols of diagnosis and treatment of diseases such as MDR non-typhoidal Salmonella spp.

Reply #2:

Yellow mark: Cases of such broad resistance in non-typhoidal *Salmonella spp.* are extremely rare in the western world and, to our knowledge, have not been reported in Europe so far. This was also stated in line 65/66 of the abstract.

Green mark: The case report was written from an interdisciplinary perspective. Since the close cooperation between clinician gastroenterologists, infectiologists and microbiologists was stressed in several sections, our case report might resemble a valid protocol for empirical treatment in patients with travel history and predisposing biliary disease.

Comment #3: This case report is acceptable for publishing.

Reply #3: We thank you very much for your kind recommendation.

We hope that our replies help to explain how occurrence of multi-drug resistance can be especially harmful in patients with predisposing liver diseases, and how these patients can effectively be treated. We hope that we will meet your requirements to make this crucial issue accessible for a broad readership.

Sincerely yours,

Dr. Philip Ferstl