September 30, 2014

Dear Editor,

Please find attached the edited manuscript in Word format (file name: 13504-edited.doc). I am unable to re-submit our revised manuscript and other necessary documents as your provided address http://www.wjgnet.com/esps/ModifyManuscript.aspx?UserId=w7hby62qz4HQHH1D4OmKuWI%2fytFn83dSU9YeWIzrB7g%3d&id=QUNNMcuAU9DjPh3DCF%2b1hg%3d%3d&UserNumId= is not working.

Title: Evidence-based Consensus on the diagnosis, prevention and management of HCV disease

Author: Mahrukh Akbar Shaheen, Muhammad Idrees

Name of Journal: *World Journal of Virology*

ESPS Manuscript NO: 13504

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

Reviewer # *02445121*:

COMMENT:

In this review, the author provide an overview of the current evidence-based consensus on the diagnosis, prevention and management of HCV disease. This review is described in detail, which, as a valuable information, could help the readers that have better understand the first-hand knowledge of this topic to start novel studies.

RESPONSE:

Thanks to Reviewer-02445121 for appreciating this review article as "First-hand knowledge".

COMMENT:

It is suggested that the contents of "Management of HCV infection" should be supplemented the research progresses on the new anti-viral drugs in the treatment of chronic hepatitis C, such as direct-acting antiviral agents (DAA), including Boceprevir, Danoprevir, TMC435, Mericitabine (RG-7128), Tegobuvir (GS-9190), Daclatasvir (BMS-790052), etc. In addition, the research progresses on the multi drug regimen （i.e. IFN-free） for HCV infection should be also updated.

Response:

Suggestion well taken and incorporated. We have added more information regarding direct acting anti-viral agents as suggested (highlighted in the manuscript). The modifications appears in the manuscript as follows:

"A new era of direct acting anti-HCV agents

Though the current standard therapy for chronic HCV infected patients is pegylated interferon-α in combination with ribavirin, however, a number of side effects of the current standard therapy usually make adherence to treatment difficult and reducing an SVR[91].

A new era of direct acting anti-viral (DAA) defined as agents/compounds that interfere with specific steps in the HCV life cycle through a direct interaction with the HCV encoded polyprotein and its cleavage products has emerged. To elevate SVR, DAAs are given in combination to the existing standard of care (pegylated interferon and ribavirin) for chronic hepatitis C infected patients with genotype 1 infection. Of these DAAs, 2 protease inhibitors, telaprevir and boceprevir, are in use for HCV treatment since 2011[92]. Other DAAs recently in use are TMC-435, vaniprevir, BI-201335, BMS-650032, Mericitabine (RG-7128), Tegobuvir (GS-9190), Daclatasvir (BMS-790052) and danoprevir. However, treatment outcome shows an overall efficacy rates between 70%-90% in no improvement in side effects.

Recently several other anti-viral agents are developed that directly target various stages of HCV replication and are proved very effective interferon-free therapy for HCV-infected patients[93]. Of these, the most important is oral nucleotide analogue 'Sofosbuvir' (also known as GS-7977) that is an inhibitor of the HCV nonstructural protein 5B (NS5B) RNA-dependent RNA polymerase enzyme and is very effective against HCV. Sofosbuvir was recently approved for use in combination with ribavirin and/or pegylated interferon for chronic HCV infection, depending on the genotype. The recommended regimens and duration of therapy for genotype 1 or 4 chronic hepatitis C is: Sofosbuvir, peginterferon alfa, and ribavirin for 12 weeks; for genotype 2: Sofosbuvir and ribavirin for 12 weeks; for genotype 3: Sofosbuvir and ribavirin for 24 weeks; for hepatocellular carcinoma awaiting liver transplantation: Sofosbuvir and ribavirin for up to 48 weeks or until liver transplantation (whichever occurs first). Sofosbuvir and ribavirin oral therapy is very effective against genotypes 2 and 3 HCV infections[94]."

Reviewer #*02444986*:

authors aimed to review strategies for prevention of hcv infention among IDU but they talk about all aspects of hcv infection i.e diagnosis, treatment, even transplantation. furthermore, there is nottting original.

Response:

We invite the Reviewer#02444986 to review the manuscript and then give his/her comments. We believe that this manuscript covers all the aspects not the IDU. In addition, we have modified the manuscript and now we feel the paper is improved considerably following extensive efforts to insure a more modifications and attention to the reviewers' comments.

Reviewer #*00504581*:

there is an interesting and well done review of the different issues related with the virus C

Response:

Thanks to reviewer for appreciating this study.

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

Sincerely yours,

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