Reviewer's report

Title: The high comorbidity burden of the Hepatitis C Virus infected population in the United States

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Reviewer: Gokul C. Das

Reviewer's report:

Over 180 million individuals globally and 4 million alone in the US are infected with HCV that is an etiologic agent for chronic hepatitis, cirrhosis, hepatocellular carcinoma and end-stage liver disease along with other extra-hepatic diseases. The current standard therapy-interferon alpha plus ribavirin is effective only about 50 percent of the cases and it is again genotype specific. HCV induces insulin resistance in chronically infected patients and development of IR contributes to the non-response to therapy and progression of the liver disease. In addition to hepatic disease, several non-hepatic diseases are associated with HCV infection including type 2 diabetes mellitus, cryoglobulinemia, steatosis, non-alcoholic liver disease etc. Many comorbid conditions are present in HCV infected patients, probably serving as a cause of infection or the effect and affects not only the treatment decision but also the outcome. Therefore, it is highly significant to understand the presence of comorbid conditions for the development of effective therapeutic strategy. This manuscript is developed certainly on an important issue..The title and abstract reflect correctly the contents, but writing needs improvement for clarity, smooth reading.

Major Compulsory Revision:

The major problems with this study are the following:

1. Although the authors attempted to estimate systematically the top 25 comorbid conditions in the US population, it appears as a biased selection of population within the US medical claim data base of integrated Health Care Information System based on medical coverage and submission of medical claims.

2. Again, it is only for a period of two years.

3. The prevalence of liver disease (other) came out as number one (37.5%) in the list of top 25 comorbid conditions. How the authors rule out that it is not the effect of HCV infection?

3. Epidemiological study suggest that the incidence of type 2 diabetes is about 3 times more among chronically infected individuals and it is supported by HCV’s ability to induce insulin resistance, a hall mark of metabolic syndrome. Diabetes
milletus came out as number 23 in the list of comorbid conditions. that does not provide me enough confidence about the design of statistical analysis and/or selection of study group.

4. Coinfection with other viruses, particularly HCV/HIV or HCV/HBV are very common (about 30%), this is also at the bottom of the list that make me uncomfortable with this analysis.

5. No information of genotypes, ethnic groups and ages associated with the comorbid conditions are provided.

Minor Essential revisions

Legends of Fig 1 needs more work for clarity.

Discretionary Revisions:

While the objective of this study is highly significant in the field of HCV research, the selection of data base and analysis has limitation. An appropriate data base should be selected and both treated and untreated patient information with age and ethnicity should be included along with infected and uninfected population.