

**Prof. Lian-Sheng Ma, Founder and Chief Executive Officer
Of World Journal of Gastroenterology
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Dear Doctor Lian-Sheng Ma,

We re-submit to your attention our invited mini-review article “**Epidemiological and clinical aspects of HBV infection in Italy over the last 50 years**” (Number ID: 02942289).

The manuscript has been improved according to the suggestions of the reviewers. The changes are shown underlined in the new manuscript.

Reviewer 1, 03725279 Minor revision

This manuscript summarizes the epidemic trend and prevention measures of hepatitis B virus in Italy in the past 50 years, and the challenges faced in recent years. This manuscript is of great scientific significance for scholars to understand the status of hepatitis B virus in Italy.

Reviewer’s Point 1: It is recommended that the authors add contrast in HBV status and control measures with the country with large HBV patients (e.g., China), thereby providing readers with a better understanding of the present situation in Italy.

Answer to the Reviewer point 1: The suggestion of the reviewer has been accepted and data from China were included in the new manuscript.

Reviewer’s point 2: In Table 1, why did the author choose 0-14 years old, 15-24 years old, 25-34 years old, 35-54 years old and ≥ 55 years old for grouping? Does this grouping have specific scientific significance?

Answer to the Reviewer point 2: The reviewer made a fair observation. However, the data reported are those elaborated of the SEIVA program of the Italian Superior Institute of Health, technical institute of the Italian Ministry of Health, made available to doctors and researchers but not further processable.

Reviewer’s point 3: It is suggested that the data in Table 1 should be transformed into a line chart to make it more readable after more scientific adjustment of age grouping.

Answer to the Reviewer’s point 3: We tried to transform table 1 into a line chart with little success due to the excessive overlapping of lines especially below the incidences of 1/100,000 inhabitants.

The manuscript has been completely revised and some confounding elements removed. The conclusion has been expanded, reorganized and made more homogeneous.

Reviewer 2, 02592404 Accept (General priority)

In this paper, Sagnelli et al. summarized epidemiology of HBV infection in Italy. They described that HBV infection decreased gradually after introducing several policies such as universal vaccination and educational campaigns. Additionally, they mentioned the negative effects of COVID-19 pandemic on the trend towards HBV eradication. The manuscript is written well but I have some specific comments as below.

Reviewer's point 1: The incidence rate of acute hepatitis B in Italy is shown in Table 1. Additionally, please make another table that summarizes HBsAg-positive rate in different area and different years with appropriate references. It would be helpful to understand the tendency of HBV epidemiology in Italy.

Answer to the Reviewer's point 1: We included Figure1 in the new manuscript to summarize the HBsAg-positive rate in different area and different years; the appropriate reference was also reported.

Reviewer's Point 2: It is described that COVID-19 pandemic has interrupted the trend towards HBV eradication, but data showing this interruption is not mentioned enough. Please show more data on this point with appropriate references.

Answer to the Reviewer's point 2: In accordance with the reviewer's suggestions, we have added information on what was requested.

Reviewer's point 3. In the abstract, please correct "COVID-19 C pandemic" to "COVID-19 pandemic".

Answer to the Reviewer point 3: The observation of the reviewer has been accepted and the manuscript was modified accordingly.

Reviewer's point 4: Please spell out abbreviations such as "SARS-CoV2" and "COVID-19" when appear first in the main text.

Answer to the Reviewer point 4: The observation of the reviewer has been accepted and the manuscript were modified accordingly.

The manuscript has been completely revised and some confounding elements removed. The conclusion has been expanded, reorganized and made more homogeneous.

Reviewer 3, 03656599 Rejection

This manuscript analyzes the changes of hepatitis B epidemiology in Italy in recent years and the causes of the changes, but I think it is not suitable for publication now. The content of the study is too superficial and it is not innovative enough, either. It only mentions the incidence of hepatitis B without involving other indicators, and the reasons affecting the epidemiology mentioned are well known, so it cannot point out the direction or focus of future research for clinical or scientific research. The data explanation part of the article is not clear enough, and it would be better to figures to reflect the decline in hepatitis B prevalence caused by immigration, hepatitis B vaccine or other factors. More data should be provided on the limited diagnosis and treatment of HBV patients as a result of COVID-19.

Answer to reviewer number 3: Following the reviewer's criticisms we have better represented the influence of hepatitis B vaccination and migration flows on the epidemiology of hepatitis B in Italy, provided more data on the limitations imposed by the COVID-19 pandemic on diagnosis and treatment of HBV hepatitis. Indicators, and the reasons affecting the epidemiology have been mentioned. We also gave some pointers for future clinical and scientific research. The manuscript has been completely revised and some confounding elements removed. The conclusion has been expanded, reorganized, and made more homogeneous.

The manuscript has been read and approved by all the authors and has not been submitted for publication to other journals. We also declare that we have no conflict of interest in connection with this paper. Neither the manuscript nor part of it has been published or is under consideration for publication elsewhere.

We hope that this paper will be found worthy of publication in the *World Journal of Gastroenterology*.

Yours sincerely,

Prof. Caterina Sagnelli