To reviewer 00030389:

Thanks for your comments, our modifications are as follows, and are marked with green background at the corresponding position in the manuscript. The yellow background marks the modifications to another Reviewer.

We can't upload the manuscript we marked under the file designation of " Manuscript File ", we have no choice but to upload the manuscript under the file designation of "Image File", please download "Image File" file. We apologize for the inconvenience we caused.

#1. P10, lines 303-304. "the vaccine has been effective in preventing HBV transmission to newborns." The authors should present the prevalence of HBV in the people aged <30 years. They only showed that HBV patients aged <30 years are minority in the patients studied in this study.

Response #1:

Due to the fact that the all the sample of our study is HBV serums, it is not possible to estimate the prevalence of HBV in the general population aged <30 years. We cited articles studying the prevalence of HBV in different age groups to prove this conclusion on the line 308-310 as" According to China Center for Disease Control, HBsAg prevalence among 1-4, 5-14, and 15-29 years old general population was 9.9%, 10.6% and 9.8%, respectively in 1992. Which declined to 0.3%, 0.9% and 4.4%, respectively in 2014." And indicate that our data can only indirectly support this conclusion on the line 312-313 as" Our data indirectly verifies this conclusion, the majority (91.19%) of HBV mono-infected patients falling between 31 and 70 years old, among which distributed relatively even."

#2. P10, lines 308-312. "At that time, the prevalence of HBV and HDV was slightly higher among adults (currently in the 51-80 years age group) who were naturally infected, and most minors (currently in the 31-50 years age group) may have been infected through intrafamilial transmission. Since HDV requires HBV for secretion and infection [25], HBV vaccination is effective in preventing HDV transmission to newborns." The authors did not succeed to describe the reason why HDV prevalence in the patients aged >50 was higher than in those aged <50.

Response #2:

We describe the reason as in 1992, along with HBV vaccination widespread, the awareness about viral hepatitis prevention was improved too. So, when HBV patients aged 31-50 became adults, risk behaviors such as unsafe sexual contact or injection were declined compared to 51-80 years age HBV patients. The detail description is on the line 316-323 as "Before 1992, the health, medical and hygiene conditions of China were suboptimal, and the awareness about viral hepatitis prevention was poor. HDV infected Chinese adults (currently in the 51-80 years age group) severely through risk behaviors such as unsafe sexual contact and injection, and infected minors (currently in the 31-50 years age group) occasionally through intrafamilial transmission. In 1992, along with HBV vaccination widespread and economic development, the suboptimal conditions and the aware-ness about viral hepatitis prevention were improved too. When HBV patients aged 31-50 became adults, the decline of risk behaviors might be one of the reasons for their relatively low HDV positive rate."

#3. P10, lines 317-320. "As we previously reported, most hepatitis D patients in Jilin Province were infected with HDV Genotype 1 [18], which secretes high virus titers with extremely delayed kinetics [26], providing patients with more time to respond to the virus." The authors did not succeed to describe the reason why the positive rate of HDV RNA among anti-HDAg positive patients in Jilin Province is relatively low.

Response #3:

Based on our current study data, we are unable to obtain the accurate reasons for this phenomenon. We will collect anti-HDAg positive samples from other regions to study the differences in HDV positive rates among anti-HDAg positive patients, and the reasons for the differences of positive rates.

Based on our previous study data, we describe the speculation on the line 330-333 as" More research is needed to understand it, one possible reason was, as we previously reported, most hepatitis D patients in Jilin Province were infected with HDV Genotype 1 [18], which secretes high virus titers with extremely delayed kinetics [27]. The delay of HDV secretion providing patients' immune system with more time to respond to the HDV before it proliferates extensively and widespread."

#4. P10, 328-329. "Additionally, we found that among anti-HDAg positive patients, the HDV RNA positive rate was positively correlated with the HBsAg level, except for an abnormal increase in the $1X10^3$-$1X10^4$ group." This sentence is incorrect and not based on the statistical analysis. The true finding must be that the HDV RNA positive rate was positively correlated with the HBsAg level, except for an abnormal decrease in the $1X10^4$-$1X10^5$ group.

Response #4:

Thank you for your valuable suggestions, we have corrected it as" except for an abnormal decrease in the $1X10^4$-$1X10^5$ group" on the line 342.

#5. P10, lines 329-333. The authors did not succeed to describe the reason why the levels of HBsAg and HBV DNA of the HDV-resolved patients were significantly lower than the HBV mono-infected patients.

Response #5:

We speculate it may due to their strong immune systems, which can maintain the HBsAg on low level and resolving HDV acute infection in the same time. We modified on the line 344-347 as "We speculate that, before HDV acute infecting those HDV-resolved patients, their immune systems maintain the HBsAg on low level already, and were more capable of resolving HDV acute infection than those who with high level HBsAg. Otherwise, HDV-resolved patients might eliminate HDV alone with some HBV after HDV acute infection, leading to decrease in HBsAg and HBV DNA."

#6. P10, lines 345-346. In this study, the authors did not study the severity of the diseases.

#7. P11, lines 362-364. In this study, the authors did not study the severity of the diseases.

#11. The authors should present the clinical characteristic of the patients studied, especially antiviral treatment.

Response #6 #7 #11:

Thank you for your valuable suggestions. In accordance with the ethical approval requirements of the project, we can only collect information such as HBsAg, HBV DNA, anti-D and HDV RNA of our specimens. I'm sorry that we can't get the information such as the severity of the diseases and patients' antiviral treatment, and therefore can't do the relevant analysis. If possible, we will reapply for ethic to obtain relevant information in the future.

#8. P11. The authors should describe the conclusion based on the results of this study.

Response #8:

We added conclusion on the line 377-386 as "In Jilin Province, China, the prevalence of anti-HDAg was 3.6% and the prevalence of HDV RNA was 1.2% among hepatitis B patients. These rates were related to age, and the majority of hepatitis D patients were 51-70 years old. The experimental data suggests that screening for HDV infection is more likely to yield positive results in hepatitis B patients with lower HBV DNA level. Patients with lower HBsAg levels ap-pear to resolve HDV acute infection, while those with higher anti-HDAg levels are more likely to test positive for HDV RNA. A weak correlation was observed between HBsAg and anti-HDAg in hepatitis D patients. Overall, our study highlights the importance of considering multiple factors when assessing the severity of HDV infection, comprehensive evaluation of patients' clinical and laboratory parameters is necessary for proper diagnosis and treatment."

#9. Abstract. "Hepatitis B patients with lower HBsAg levels appeared to be more capable of resolving HDV acute infections, while patients with higher anti-HDAg levels were more likely to test positive for HDV RNA." This description is the interpretation of the authors. They should describe the results.

Response #9:

We changed the description on the line 27-28 as" Among anti-HDAg positive patients, the HDV RNA positive rate was positively correlated with the HBsAg level and anti-HDAg level."

#10. Abstract. The authors should describe the conclusion at the end of abstract.

Response #10:

We added the conclusion on the line 29-31 as" Our study highlights the importance of considering multiple factors when assessing the severity of HDV infection, comprehensive evaluation of patients' clinical and laboratory parameters is necessary for proper diagnosis and treatment."

To reviewer 03488616:

Thanks for your comments, our modifications are as follows, and are marked with yellow background at the corresponding position in the manuscript. The green background marks the modifications to another Reviewer.

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1- The abstract lacks several information about age and gender distribution of the patient group, the results in the abstract lacks any information about relation of HBV/HDV coinfection with age, however it is mentioned in the title.

Response 1-:

We added age and gender distribution in abstract on the line 22 as" (3,293 males and 2,301 females, age range of 2 to 89 years)", and information about relation of HBV/HDV coinfection with age on the line 25-26 as" 87.69% of hepatitis D patients were 51-70 years old".

2- The title should include " in Chinese patients" as the the work is limited by the generality or generalization of results.

Response 2-:

We modified the title as "Hepatitis D virus dual-infection among Chinese hepatitis B patient related to hepatitis B surface antigen, hepatitis B virus DNA and age"

3- In the methods, blood collection and serum separation should be mention in detail. Also, mention the amount of serum used for HBV DNA and HDV RNA extraction.

Response 3-:

We added blood collection and serum separation on the line 86 as" Fasting venous blood was centrifuged at 4000 rpm for 10 min to obtain serum." And added the amount of serum used for HBV DNA and HDV RNA extraction on the line 99 as" 400ul serum were used to detect HBV DNA by the Roche COBAS AmpliPrep/COBAS TaqMan system" and on the line 110-111 as" We selected anti-HDAg-positive specimens and used a nucleic acid extraction reagent (Jianwei, Shandong, China) to extract nucleic acid from 400ul of serum"

4- Other clinical and laboratory data e.g., liver function tests for the patients should be tabulated. The study also may benefit from correlation between the investigated parameters with lab data.

Response 4-:

Thank you for your valuable suggestions. In accordance with the ethical approval requirements of the project, we can only collect information such as HBsAg, HBV DNA, anti-D and HDV RNA of our specimens. I'm sorry that we can't get the liver function and therefore can't do the relevant analysis. If possible, we will reapply for ethic to obtain relevant information in the future.