Clinical and Experimental Obstetrics & Gynecology

*Clin. Exp. Obstet. Gynecol.* **2022**; 49(1): 004
http://doi.org/10.31083/j.ceog4901004

*Original Research*

# Analyzing the detrimental effects of female chronic hepatitis B virus DNA on ovarian reserve function and results of *in vitro* fertilization

Liu Liu[1], Hua Liang[1], Jing Yang[2,*,†], Fujin Shen[1,*,†], Wei Li[1]

[1]Department of Obstetrics and Gynecology, Renmin Hospital, Wuhan University, 430074 Wuhan, Hubei, China
[2]Reproductive Medicine Center, Renmin Hospital, Wuhan University, 430074 Wuhan, Hubei, China
*Correspondence: dryangqing@hotmail.com (Jing Yang); shenfj_rmh@outlook.com (Fujin Shen)
[†]These authors contributed equally.

Academic Editor: Michael H. Dahan
Submitted: 26 December 2020 Revised: 11 February 2021 Accepted: 24 February 2021 Published: 7 January 2022

**Abstract**

**Background**: To evaluate both the impact of hepatitis B virus (HBV)-DNA copies in women with HBV infection on the ovarian reserve function and outcomes of *in vitro* fertilization (IVF). **Methods**: We conducted a retrospective study on a total of 9927 couples undergoing their first IVF cycle. After filtering, 1570 couples (546 HBV-seropositive women and 1024 HBV-seronegative women whose partners were HBV-seronegative) failed to meet inclusion criteria. According to the HBV-DNA titers in serum, the HBV-seropositive group was divided into three groups: DNA-high copy group (n = 139), DNA-low copy group (n = 241), and DNA-negative group (n = 166). All patients underwent controlled ovarian hyperstimulation using the long downregulation protocol followed by IVF. **Results**: Compared with the HBV-negative group, HBV-positive women with high DNA copy exhibited lower antral follicle count (AFC) (11.9 $\pm$ 4.3 vs 13.3 $\pm$ 3.2), lower number of oocyte retrieved (9.2 $\pm$ 5.7 vs 13.1 $\pm$ 6.1), larger proportion of AFC $<$8 (7.9% vs 3.1%) and anti-mullerian hormone (AMH) $<$2 $\mu$g/L (8.6% vs 4.3%). Both high-DNA copy and low-DNA copy groups exhibited a lower fertilization rate (70.9% and 72.5% vs 75.1%), lower high-grade embryo rate (51.5% and 53.8% vs 56.9%), lower implantation rate (31.3% and 32.7% vs 38.5%), lower clinical pregnancy rate (40.3% and 42.3% vs 49.6% per cycle with OR; 45.5% and 48.8% vs 56.8% per cycle with ET) than the HBV-negative group. Moreover, a higher early abortion rate (19.6% and 15.7% vs 7.1%) was observed in the above two groups. **Conclusion**: HBV-DNA may have a negative effect on women's ovarian reserve function which in turn results in poor fertilization rate, clinical pregnancy rate and high early abortion rate in IVF treatment.

**Keywords:** HBV-DNA; Female infertility; Ovarian function; *In vitro* fertilization

## 1. Introduction

Chronic hepatitis B virus (HBV) infection, which can cause hepatic inflammation and severe diseases such as hepatocirrhosis and hepatocellular carcinoma, is a worldwide public health concern [1]. It is estimated that a global prevalence of 3.5% [2], i.e., 2.57 billion people worldwide have been infected with HBV and that roughly 270 million people have been chronically infected, of whom women of reproductive age account for 25.3% [3]. China accounts for some of the highest prevalence of HBV around the world [4,5]. The main source of transmission for HBV is via familial vertical transmission, including cases of both mother- and father-to-infant vertical transmission, the former being dominant [6–8]. Newborns from HBsAg positive pregnant women who begin passive-active immunization immediately after birth can significantly reduce vertical transmission, but still have 5%–10% infection with HBV [9,10].

Hepatitis B virus is a double-stranded DNA virus of the Hepadnaviridae family. Serum HBV-DNA content is the most direct and reliable indicator of viral activity in HBV-infected patients [11,12]. Apart from hepatocytes, HBV-DNA is also found and expressed in reproductive gonads, such as testis, sperm, seminal plasma, granulosa cells, and oocytes [13]. One study reported that HBV-DNA high-level mothers are more susceptible to mother-to-child transmission [14]. Furthermore, HBV can infect spermatozoa, which in turn affects its quality and function [15]. Recently, as an increasing number of HBV seropositive infertile couples have chosen ART, certain challenges have emerged: could chronic HBV infection affect the ovarian reserve function, egg quality, embryonic development, embryo quality, and pregnancy outcome of *in vitro* fertilization (IVF) and embryo transfer (ET)?

Given that the cases in our medical center have been routinely and systematically screened for both partners for repertoire virus prior to IVF treatment, we undertook a retrospective study to evaluate the impact of HBV-DNA on ovarian function, ovarian stimulation and outcome of IVF for women with or without infection by HBsAg.

## 2. Materials and methods

### *2.1 Patients*

This study included 9927 infertile couples (20–43 years of age) seeking IVF treatment for the first cycle from October 2014 to August 2019 in the Reproductive Medical Center of Renmin Hospital of Wuhan University. All cou-

**Table 1. Clinical characteristics of HBV-positive and HBV-negative groups.**

| Characteristics | HBV-positive groups | | | HBV-negative group |
|---|---|---|---|---|
| | DNA-high copy | DNA-low copy | DNA-negative | (n = 1024) |
| | (n = 139) | (n = 241) | (n = 166) | |
| Female age (years) | 31.2 ± 4.0 | 31.2 ± 4.6 | 31.3 ± 3.1 | 30.9 ± 4.2 |
| Male age (years) | 35.1 ± 5.5 | 35.0 ± 4.0 | 34.8 ± 4.7 | 34.2 ± 4.8 |
| Female BMI (kg/m$^2$) | 21.9 ± 2.8 | 21.9 ± 2.3 | 21.8 ± 2.7 | 21.8 ± 3.0 |
| Male BMI (kg/m$^2$) | 23.3 ± 3.2 | 23.6 ± 3.4 | 23.4 ± 3.1 | 23.3 ± 3.3 |
| Duration of infertility (years) | 4.5 ± 3.6 | 4.4 ± 2.5 | 4.3 ± 2.8 | 4.20 ± 3.2 |
| Cause of infertility | | | | |
| Tubal blockage | 114 (82.0%) | 192 (79.7%) | 134 (80.7%) | 811 (79.2%) |
| Male factor | 40 (28.8%) | 73 (30.3%) | 47 (28.3%) | 267 (26.1%) |
| Others | 6 (4.3%) | 12 (5.0%) | 8 (4.8%) | 41 (4.0%) |
| Basal semen parameters | | | | |
| Volume (mL) | 1.89 ± 0.7 | 1.81 ± 0.5 | 1.83 ± 0.4 | 1.85 ± 0.6 |
| Concentration (× 10$^6$/mL) | 76.24 ± 47.2 | 75.24 ± 45.1 | 76.01 ± 47.6 | 75.35 ± 46.9 |
| Progressive motility (a + b) (%) | 30.4 ± 18.8 | 30.9 ± 16.8 | 30.7 ± 18.2 | 29.98 ± 17.6 |
| Normal morphology (%) | 14.58 ± 4.9 | 14.31 ± 4.5 | 13.9 ± 5.2 | 14.01 ± 5.5 |

Note: Values are presented as mean ± SD or numbers (percentages) of participants.

ples were tested for repertoire viruses such as HBV, HCV, HIV and syphilis within 1 year of the ART cycle during routine HBV-DNA inspection in patients with Serum HBsAg positive. HBV-seropositive patients with DNA titers $>1 \times 10^6$ IU/mL were suggested antiviral treatment before ART. Couples who were seropositive for HCV, HIV, syphilis or those who were diagnosed with acute hepatitis, obvious liver dysfunction or who had received any antiviral therapy before cycles were excluded from the study. We further excluded couples with chromosomal abnormalities, women with a history of endometriosis, ovarian surgery, and whose partners had been diagnosed with asthenospermia and azoospermia. Additionally, HBV-seropositive male partners were screened out. All male partners had semen analysis conducted after 3–7 days of sexual abstinence. Semen parameters were analyzed according to WHO guidelines (5th edition) [16].

Based on the above inclusion and exclusion criteria, we excluded 8357 infertile couples and screened out 1570 infertile couples for investigation, among whom, all male partners were HBV-seronegative. According to the criterion whereby HBsAg is positive or not and the HBV-DNA titers in serum of female partners, the patients were divided into four groups, HBV-DNA-high copy group (n = 139): serum HBsAg (+), HBV-DNA $>1 \times 10^5$ IU/mL; HBV-DNA-low copy group (n = 241): serum HBsAg (+), 500 IU/mL <HBV-DNA $<1 \times 10^5$ IU/mL; HBV-DNA-negative group (n = 166): serum HBsAg (+), HBV-DNA <500 IU/mL; and HBV-negative group (n = 1024): serum HBsAg(-). The male partners for all groups were seronegative for HBsAg.

### *2.2 The ART treatment protocol*

All patients underwent IVF treatment with routine pituitary suppression protocol, as previously described [17]. In brief, patients were subcutaneously injected with gonadotropin-releasing hormone agonist (GnRH-a; Decapeptyl or Diphereline; Ispen, Paris, France) in the mid-luteal phase for at least 14 days. Once the pituitary activity was completely suppressed, the process of ovarian stimulation was commenced with human menopausal gonadotropin (hMG; LIVZON Group, Guangzhou, China) or recombinant follicle-stimulating hormone (FSH; Gonal-f; Merck Serono, Geneva, Switzerland or Puregon; Schering-Plough; Kenilworth, NJ, USA). Human chorionic gonadotropin (HCG; LIVZON Group, Guangzhou, China) was injected when at least three follicles had an average diameter of 18 mm. Then, the oocytes were retrieved after HCG had been injected for 34–36 hours. In the following 16 to 20 hours, IVF was conducted, followed by embryo selection and ET after being cultured *in vitro*. If there were no available embryos or in the event that patients developed OHSS or showed a risk of OHSS, cycles were canceled.

### *2.3 IVF outcome measures*

Basic data of patients included: age and BMI of couples; sperm parameters; duration and cause of infertility; ovarian reserve evaluation (levels of serum anti-mullerian hormone, menstrual cycle day 3 levels of serum FSH, LH, $E_2$ and antral follicle count). We also collected data con-

**Table 2. The data on ovarian reserve function of HBV-positive and HBV-negative groups.**

| Characteristics | HBV-positive groups | | | HBV-negative group |
|---|---|---|---|---|
| | DNA-high copy | DNA-low copy | DNA-negative | (n = 1024) |
| | (n = 139) | (n = 241) | (n = 166) | |
| FSH level (IU/L) | 7.6 ± 1.7 | 7.4 ± 1.8 | 7.1 ± 2.0 | 7.3 ± 2.2 |
| LH level (IU/L) | 4.7 ± 2.1 | 4.7 ± 2.9 | 4.6 ± 2.2 | 5.0 ± 3.6 |
| $E_2$ level (IU/L) | 48.9 ± 15.4 | 49.4 ± 18.1 | 48.5 ± 16.8 | 45.6 ± 14.2 |
| No. of AFC | 11.9 ± 4.3* | 12.8 ± 5.5 | 13.1 ± 4.6 | 13.3 ± 3.2 |
| FSH >10 mIU/mL | 8 (5.8%) | 13 (5.3%) | 8 (4.8%) | 53 (5.2%) |
| FSH/LH >3 | 16 (11.5%) | 25 (10.4%) | 16 (9.7%) | 123 (12.0%) |
| AFC <8 | 11 (7.9%)** | 12 (5.0%) | 6 (3.6%) | 32 (3.1%) |
| AMH <2 $\mu$g/L | 12 (8.6%)* | 17 (7.1%) | 9 (5.4%) | 44 (4.3%) |

Note: Values are presented as mean ± SD or numbers (percentages) of participants.

*$p < 0.05$, versus HBV-negative group (Mann-Whitney U-test or Chi-squared test).

**$p < 0.01$, versus HBV-negative group (Chi-squared test).

cerning COH and embryology: duration and total dose of gonadotropin (Gn) applied; serum estradiol ($E_2$) lever and endometrial thickness on the day of HCG injection; the number of oocytes retrieved and embryos transferred; cycles with rescue ICSI performed; cycles without ET for no viable embryos; cycles without ET for the danger of OHSS; fertilization rate; high-grade embryo rate; implantation rate; pregnancy rate; early abortion rate.

Fertilization rate was defined as the number of confirmed zygotes per the number of oocytes retrieved in the IVF cycle. High-grade embryo rate was defined as the number of embryos having ≥6 cells with a type of A or B per number of divisive embryos on day 3 of culture. Implantation rate was represented by the number of intrauterine or extrauterine gestational sacs checked by vaginal ultrasound examination 30 days after embryo transfer per embryo transferred. Clinical pregnancy rate was defined as the number of women who had intrauterine gestational sacs per cycle with oocyte retrieval or embryo transfer. Early abortion rate was defined as the number of cycles of abortion per number of cycles of all clinical pregnancies within 12 weeks.

### *2.4 Statistical analyses*

Data were reported as mean ± standard deviation (SD) for continuous variables and percentage for categorical data. All statistical analyses were conducted using the commercial software Statistical Package for Social Science, v.22.0 (SPSS Inc., Chicago, IL, USA). Continuous variables and categorical data between two groups were analyzed statistically by independent sample *t*-test and Chi-squared test, respectively. All *p* values quoted were two-sided, and *p* value $< 0.05$ was considered as statistically significant.

## 3. Results

At the outset of this study, we analyzed a total of 9,927 couples (20–43 years of age) who underwent their first IVF cycle in our medical center from October 2014 to August 2019, among whom 596 (6.0%) were HBsAg positive, with the prevalence of HBsAg of each year shown in Fig. 1.

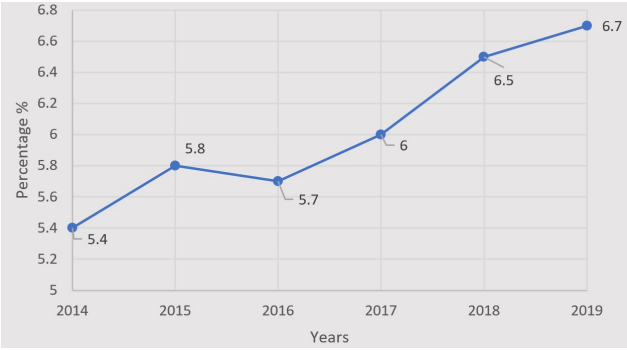


**Fig. 1. Prevalence of women positive for HBsAg from 2014 to 2019 in our medical center.**

Based on inclusion and exclusion criteria, we excluded 8357 infertile couples and screened out 1570 infertile couples, among whom 546 women were HBsAg positive with 139 women categorized as high DNA copy and 241 women as low DNA copy. The demographic data of the subjects are shown in Table 1. Regarding the indexes of age, BMI of couples, the duration and cause of infertility, and the basal semen parameters, there were no significant differences between the HBV-positive and HBV-negative groups ($p > 0.05$). Additionally, there were no significant differences ($p > 0.05$) among the three HBV-positive groups for these indexes.

**Table 3. The data on COH and embryology of HBV-positive and HBV-negative groups.**

| Characteristics | HBV-positive groups | | | HBV-negative group |
|---|---|---|---|---|
| | DNA-high copy | DNA-low copy | DNA-negative | (n = 1024) |
| | (n = 139) | (n = 241) | (n = 166) | |
| Duration of Gn stimulation (d) | 11.0 ± 1.3 | 10.9 ± 1.9 | 11.1 ± 1.5 | 10.5 ± 1.0 |
| Total dose of Gn used (IU) | 2287.9 ± 730.2 | 2295.38 ± 642.5 | 2310.36 ± 814.2 | 2340.48 ± 763.1 |
| Endometrial thickness (mm) on the day of HCG injection | 1.1 ± 0.7 | 1.0 ± 0.5 | 1.1 ± 0.9 | 1.0 ± 0.2 |
| $E_2$ level (pg/mL) on the day of HCG injection | 4512.6 ± 2116.4 | 4463.54 ± 3320.7 | 4481.02 ± 3926.4 | 4532.23 ± 4518.9 |
| No. of oocytes retrieved | 9.2 ± 5.7* | 12.6 ± 5.1 | 13.0 ± 6.4 | 13.1 ± 6.1 |
| No. of embryos transferred in cycles by ET | 2.03 ± 0.25 | 2.05 ± 0.41 | 2.01 ± 0.35 | 2.07 ± 0.3 |
| Cycles with rescue ICSI performed | 11 (7.9%) | 11 (7.1%) | 11 (6.6%) | 72 (7.0%) |
| Fertilization rate | 771/1087 (70.9%)** | 1571/2168 (72.5%)* | 1065/1432 (74.4%) | 5997/7985 (75.1%) |
| High-grade embryo rate | 385/748 (51.5%)** | 825/1534 (53.8%)* | 579/1042 (55.6%) | 3364/5913 (56.9%) |
| Cycles without ET for no viable embryos | 6 (4.3%)* | 9 (3.7%)* | 4 (2.4%) | 14 (1.4%) |
| Cycles without ET for danger of OHSS | 13 (8.6%) | 21 (8.7%) | 14 (8.4%) | 87 (8.5%) |
| Implantation rate | 67/214 (31.3%)* | 131/401 (32.7%)* | 107/283 (37.8%) | 750/1948 (38.5%) |
| Clinical pregnancy rate/cycle with OR | 56/139 (40.3%)* | 102/241 (42.3%)* | 80/166 (48.2%) | 508/1024 (49.6%) |
| Clinical pregnancy rate/cycle with ET | 56/123 (45.5%)** | 102/209 (48.8%)* | 80/148 (54.1%) | 508/894 (56.8%) |
| Early abortion rate | 11/56 (19.6%)** | 16/102 (15.7%)** | 8/80 (10.0%) | 36/508 (7.1%) |

Note: Values are presented as mean ± SD or numbers (percentages) of participants.

*$p < 0.05$, versus HBV-negative group (Mann-Whitney U-test or Chi-squared test).

**$p < 0.01$, versus HBV-negative group (Chi-squared test).

The data on ovarian reserve function are shown in Table 2. The AFC refers to follicles with a diameter of 2–9 mm visible in the ovary under vaginal ultrasound. It can reflect the number of original follicles remaining in the follicle pool well and is a direct reflection of ovarian reserve function [25,26]. AFC <8 is most accurate for predicting low ovarian response [27]. The number of AFC is significantly smaller in the DNA-high copy group than in the HBV-negative group (11.9 $\pm$ 4.3 vs 13.3 $\pm$ 3.2; $p = 0.037$). Moreover, the proportion of AFC <8 and AMH <2 $\mu$g/L is significantly larger in the DNA-high copy group (7.9% vs 3.1%; $p = 0.01$; 8.6% vs 4.3%; $p = 0.042$). There were no significant differences between the HBV-positive and HBV-negative groups ($p > 0.05$) for the Day 3 serum FSH, $E_2$, and LH level of menstrual cycles, the proportion of FSH >10 and FSH/LH >3. Nor were there significant differences ($p > 0.05$) among the three HBV-positive groups.

The data on COH and embryology are summarized in Table 3. We found that fewer oocytes were retrieved in the DNA-high copy group than in the HBV-seronegative group (9.2 $\pm$ 5.7 vs 13.1 $\pm$ 6.1; $p = 0.041$). Compared with the HBV-seronegative group, both DNA-high copy and DNA-low copy groups showed that more individuals cancelled ET for no available embryos (4.3% vs 1.4%; $p = 0.031$ and 3.7% vs 1.4%; $p = 0.027$), lower fertilization rate (70.9% vs 75.1%; $p = 0.003$ and 72.5% vs 75.1%; $p = 0.013$) and lower high-grade embryo rate (51.5% vs 56.9%; $p = 0.005$ and 53.8% vs 56.9%; $p = 0.029$).

The duration of Gn stimulation, total dose of Gn used, endometrial thickness on the day of HCG injection, No. of embryos transferred per ET cycle, cycles with rescue ICSI performed as well as the cycles without ET for the danger of OHSS were not significantly different among the HBV-seropositive and seropositive groups ($p > 0.05$). There were also no significant differences ($p > 0.05$) among the three HBV-positive groups.

Furthermore, compared with the HBV-negative group, the implantation rate and clinical pregnancy rates were significantly lower in both DNA-high copy and DNA-low copy groups (implantation rate: 31.3% vs 38.5%, $p = 0.039$ and 32.7% vs 38.5%, $p = 0.028$; clinical rate: 40.3% vs 49.6%, $p = 0.039$ and 42.3% vs 49.6%, $p = 0.042$ per cycle with OR and 45.5% vs 56.8%, $p = 0.018$ and 48.8% vs 56.8%, $p = 0.036$ per cycle with ET), and the early abortion rate was significantly higher in both DNA-high copy and DNA-low copy groups (19.6% vs 7.1%; $p = 0.001$ and 15.7% vs 7.1%; $p = 0.005$).

## 4. Discussion

China is a highly endemic area for HBV, with an overall prevalence of 5.2% among women of reproductive age [18]. However, the prevalence in this study was slightly higher at 5.4–6.7%, possibly on account of geographical variation. The number of seropositive infertile women in our medical center has gradually risen over the past six years, as shown in Fig. 1. Recently, laboratory tests for hepatitis B cases and clinical diagnosis have become increasingly standardized, thereby reducing the rate of missed reports. With improvements in economic conditions, more infertile women, especially in the surrounding countryside which is often at a heightened risk of hepatitis B, have embraced ART. This may further explain the higher prevalence during the study period.

In this study, 546 infertile patients infected with HBV were collected; the positive rate of HBV-DNA was 69.60% out of the total 1570 cases, among which the low copy of HBV-DNA was the majority (44.14%). This suggests that the viral replication in HBV-infected women of childbearing age is predominantly associated with low replication, that adults have a certain capacity of immune clearance of HBV, while a significant proportion of women are still highly active (DNA-high copy group: 25.46%).

Among several studies [19–23] that have addressed the reproductive performance of couples infected with HBV, results are discordant. Some studies [19,20] showed significantly lower implantation in couples conflicting for HBV infection, while others reported a higher implantation rate in couples of HBV infection than the control individuals [23]. However, none of them took into account the state of HBV-DNA copies. Our study was grouped on the copy amount of HBV-DNA, designed to evaluate the varying degrees of copy amount of HBV-DNA infection on ovarian function, ovarian stimulation and outcome of IVF for women.

In HBV-infected patients, serum HBV-DNA assay is the most direct and reliable indicator of viral activity, particularly useful in assessing the risk of disease progression and candidacy for antiviral therapy and to distinguish active hepatitis B from the inactive carrier state [24]. We found that compared with the HBV-negative group, among HBV-infected infertile women, high copy status of HBV-DNA generated fewer AFCs, a lower number of retrieved oocytes, larger proportion of AFC <8 and proportion of AMH <2 $\mu$g/L, which increases the risk of ovarian reserve dysfunction.

In women, AMH is secreted by pre-sinus follicles and small sinusoidal follicle granule cells. Compared with other existing hormone tests, AMH fluctuates slightly during the menstrual cycle and is less susceptible to gonadotropins [28]. Therefore, AMH is a sensitive and accurate indicator of ovarian reserve function [29]. AMH <2 mg/L indicates that ovarian reserve function has begun to decline [30]. AMH combined with AFC can be used as a reliable indicator for predicting ovarian reserve function [31].

Several studies have provided evidence of HBV infection in the ovaries and even in oocytes [32]. Moreover, HBV-DNA positive rates in oocytes and embryos are positively correlated with serum HBV-DNA levels [33,34]. Studies have also shown that HBV carrying can cause local immune or inflammatory reactions in the destruction of

related functions in local tissues through the deposition of antigen-antibody complexes [35–37]. HBV infection can increase the proportion of sperm cell necrosis and apoptosis, destroy the integrity of the sperm membrane, cause the loss of sperm mitochondrial membrane, and reduce the function of sperm [20]. Therefore, HBV-DNA may damage ovarian tissue and oocytes, cause changes in ovarian reserve functions such as AMH and AFC, and affect the quality of eggs and embryos. Accordingly, we postulate that when a large amount of HBV-DNA is present in the blood, it can have negative effect on ovarian reserve function.

In this study, we observed a lower fertilization rate, lower high-grade embryo rate and more cycles without ET for no available embryos in both infertile women with high and low copies of HBV-DNA. Fertilization is the process of the egg and sperm fusing into a zygote. HBV-DNA sequences may pass through the zona and oolemma and integrate with oocyte genome, and then replicate and exist in the ovum at different stages [38–41]. It may be an important mechanism for HBV vertical transmission that when oocytes are fertilized with normal spermatozoa, these sperm transmit HBV-DNA sequences to the embryo [39]. We speculate that when oocyte quality is thus damaged, the process of fertilization is affected in women with both high and low copies of HBV-DNA.

We observed lower implantation and clinical pregnancy rates in both DNA-high and DNA-low groups along with a higher early abortion rate in the above-mentioned two groups. This is consistent with the observations by Cui *et al*. [42] who showed that among 21,004 pregnant women in a prospective cohort study, the proportion of abortions in HBsAg carriers was significantly higher than in the control. Embryo is transferred in the last step of the IVF cycle and will subsequently develop into a new individual. The success rate is associated with endometrial receptivity as well as the quality of embryo. A separate study reported that integration and replication of HBV genes can cause chromosomal mutations in early embryonic cells while viral protein products can interfere with embryo metabolism and development [43]. As previously described, HBV-DNA can be detected in the female reproductive tract system and might have an impact on the embryo tissue and endometrial local immunity, and for HBV-seropositive women with impaired oocyte binding, these may be responsible (at least in part) for poor pregnancy results. In addition, we did not find differences among three HBV-positive groups, potentially attributable to insufficient sample sizes. As the sample size and research indicators of this study are still limited, large sample clinical research and related basic research are necessary to further confirm the specific underlying mechanism of this research.

## 5. Conclusions

Our study shows that HBV-DNA in HBV-seropositive women may interfere with ovarian reserve function and ultimately affect pregnancy outcome. For women of childbearing age with HBV infection, especially with high copy status of HBV-DNA, it is recommended that treatment and childbearing occur as early as possible in order to reduce the impact of HBV infection on ovarian reserve function. Prior to assisted pregnancy treatment, this population should be fully informed about possible outcomes to avoid medical risks. With enhanced prediction of ovarian reserve function, embryo quality, fertilization rate and pregnancy rate, improved consultation can be provided to HBV-seropositive infertile women.

## Abbreviations

AFC, antral follicle count; AMH, anti-mullerian hormone; ART, assisted reproductive technology; BMI, body mass index; COH, controlled ovarian hyperstimulation; $E_2$, estradiol; ET, embryo transfer; FSH, follicle-stimulating hormone; Gn, gonadotropin; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCG, human chorionic gonadotropin; HCV, hepatitis C virus; HIV, human immunodeficiency virus; ICSI, Intracytoplasmic sperm injection; IVF, *in vitro* fertilization; LH, luteinizing hormone; OHSS, ovarian hyper-stimulation syndrome; OR, oocyte retrieval.

## Author contributions

LL and HL wrote the paper and analyzed the data; FS and JY proposed the idea and help revise the manuscript; WL collected the data and provided some suggestion for drafting the manuscript.

## Ethics approval and consent to participate

The institutional review board of the Renmin Hospital of Wuhan University approved the ethics of this research (20190522002). Informed consent was obtained from all patients before data collection.


## Acknowledgment

The authors wish to thank all peer reviewers for their opinions and suggestions.

## Funding

This research received no external funding.


## Conflict of interest

The authors declare no conflict of interest.

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