A Meta–Analysis and Systematic Review to Determine the Pregnancy Outcomes in Mothers with inactive Hepatitis B Carrier

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ARTICLE INFO

Article history:
Received: 12 January, 2019
Accepted: 17 March, 2019
Online: 28 March, 2019

Keywords:
Inactive hepatitis B,
Pregnancy,
adverse effects on pregnancy

ABSTRACT

Objective: Our goal was to investigate whether asymptomatic maternal hepatitis B (HB) infection affects early membrane rupture (PROM), fetal death, preeclampsia, eclampsia, gestational hypertension, or bleeding before delivery.

Materials and Methods: This study was conducted in the Department of Community Medicine and Obstetrics and Gynecology department, KEMU Lahore for one-year duration from May 2017 to April 2018. The electronic literature surveys were conducted using gray literature studies (e.g. conference papers and final reports), (Technicians) and scanned reference lists of attached studies and systematically related studies. We study statistical heterogeneity using statistical tests I² and tau square (Tao2).

Results: 18 studies included. Early membrane ruptures (PROM), fetal death, preeclampsia, eclampsia, gestational hypertension and prenatal bleeding were obtained in this study. The results showed no significant relationship between inactive HB and these complications during pregnancy. Small amounts of P and chi-square and large amounts of I² have revealed heterogeneity, which we are trying to modify using statistical methods such as subgroup analysis in this chapter.

Conclusion: Inactive HB infection did not increase the risk of adverse effects in this study. In addition, well-designed tests should be performed to confirm the results.

Keywords: Inactive hepatitis B, Pregnancy, adverse effects on pregnancy

Introduction

Nowadays, viral hepatitis has a heavy burden on healthcare systems. As a type of hepatitis virus, hepatitis B virus (HBV) can cause worldwide morbidity and mortality(1,2). Inactive HBV is 100 times more contagious and resistant than Human Immunodeficiency Virus, and is often unnoticed (3). About 25% of sexual intercourse in Hep B infected individuals can be contagious to HBV. HBV is transmitted to an infant by an infected mother from birth, which can cause chronic hepatocellular disease or cancer in adults receiving the virus, making it a serious problem during pregnancy and motherhood (4,5). Despite vaccination against hepatitis B, HBV remains a medical and financial problem and affects young adults around the world. Virus transmission and fetal health are important issues for women around the world (6). As with many pregnancy conditions, little is known about HBV infection and it is generally accepted that inactive hepatitis B (IHB) infection did not affect pregnancy or pregnancy outcome (7). As the knowledge of the impact of Hep B on pregnancy results is important for both patients and healthcare providers, and the results of the study are controversial, we did so to partially explain the effects of this study (8).

Materials and Methods

This study was held in the Department of Community Medicine and Obstetrics and Gynecology department, KEMU Lahore for one-year duration from May 2017 to April 2018. The electronic literature searches complement scanning of gray literature search results (e.g. conference and technical report results), and scanned reference lists of relevant tests and relevant systematic reviews. We conducted a free keyword or MESH to search for the following terms: inactive hepatitis B, "hepatitis B anti-surface gene", Hbs Ag, hepatitis B carrier, pregnancy outcome, prenatal outcome, obstetric outcome, pregnancy, Premature membranous rupture (PROM), fetal death, preeclampsia, eclampsia, gestational hypertension and prenatal bleeding.
All cohorts, cases and controls and cross-sectional studies were included if one healthy control group was present and one or more results were reported. Patients who met the following criteria were included: (1) IHB carriers or pregnant women diagnosed during routine prenatal blood tests during pregnancy; (2) Pregnant women who have only one normal pregnancy without illness or drug use. (a) There is no control group of natural understanding; (b) no obstetric or perinatal results were reported; showed super-infection.

For quality assessment, we use a modified version of STROBE, which contains seven elements of the STROBE checklist (environment, participation, variables, bias, limitations and interpretation). The study included five low-risk and nine high-risk studies (Fig. 1). We used Begg and Egger tests to evaluate publication bias.

Results
The results of bibliographic studies are summarized in Figure 2. A total of 156 studies were identified and analyzed in two studies. 56 studies and 18 studies included in the meta-analysis were selected for detailed analysis. The results included in the study include:
For premature membrane rupture (PROM), six for fetal death, fourteen for preeclampsia, six for eclampsia, eight for gestational hypertension and eight for prenatal bleeding.

Meta-analysis of early membranous (ferry) rupture and inactive hepatitis B:
Eight of 18 studies compared PROM between IHB carriers and healthy pregnant women. The P value was 0.009 and the corresponding I2 statistic was 63%, suggesting moderate inter-study variability. Among women with inactive HB it was 1.33 (95% CI, 0.94-1.89) compared to women not infected with early membranous rupture. These findings suggest that there is no significant association between inactive HB carrier infection and PROM. Subgroup analysis (case control and cohort) based on study design cannot lower I2, but subgroup analysis based on study quality (high and low) can only lower I2 in low quality of the study group.

Meta-analysis of fetal death and inactive hepatitis B:
Six of 18 studies compared fetal death between HRA and healthy pregnant women. The P value was 0.08 and the corresponding I2 statistic was 50%, indicating low inter-study variability. The combined OR is 0.9, (95% CI: 0.52-1.55). This measure of effect size means that the difference between the two groups (infected and uninfected) is not statistically significant.

Meta-analysis of preeclampsia and inactive hepatitis B:
Of the 18 studies, 14 compared preeclampsia between IHB carriers and healthy pregnant women. The P value was 1.01 and the corresponding I2 statistic was 71%, indicating a significant change between studies. The risk of preeclampsia was similar in both groups (OR = 1.03, 95% CI: 0.78-1.35; for heterogeneity, we conducted two subgroup analyzes and two analyzes that could reduce the quality of study design, group and low-quality study Group.

Meta-analysis of eclampsia and inactive hepatitis B:
Six of 18 studies compared eclampsia between IHB groups and groups of healthy pregnant women (8, 20-22, 24, 31). The P value was 0.9 and the corresponding I2 statistic was 0%, suggesting no change between studies. The percentage of eclampsia was similar in both groups (OR = 1.33, 95% CI: 0.49-3.63).

Meta-analysis of gestational hypertension and inactive hepatitis B:
Eight of 18 studies compared gestational hypertension between IHB and healthy pregnant women (8, 14, 20-22, 31, 30). The P value was 0.1 and the corresponding I2 statistic was 40%, indicating low inter-study variability. The frequency of gestational hypertension was similar in the two groups (OR = 0.9, 95% CI: 0.74-1.08).

Meta-analysis of prenatal bleeding and inactive hepatitis B:
Nine of 18 studies compared prenatal bleeding between IHB and groups of healthy pregnant women (8, 12-15, 21, 23, 31, 29). The P value was 0.0002 and the corresponding I2 statistic was 74%, suggesting a small change between studies. The probability of prenatal bleeding was similar in both groups (OR = 1.13; 95% CI 0.84 to 1.51). Subgroup analysis based on study quality can lower I2 in both subgroups.

Discussion
IHB is not associated with major adverse pregnancy outcomes such as PROM before delivery, fetal death, preeclampsia, eclampsia, gestational hypertension and bleeding. However, in our interpretation, we must pay attention to the number of statistical heterogeneity tests. If we have a meta-analysis with a small sample size, the Chi2 test can detect a small heterogeneity that is not clinically significant, as in our study (9). Other parts of heterogeneity may be associated with significant differences between test results. In addition, despite the heterogeneity observed in our study, Tau2 statistics were small and amounted to 0.15. This paradox arises when the variance between studies is low and the variance in studies is high (10).
Fig. 1: Risk of bias summary: review authors' judgments about each risk.

Fig. 2: Flow diagram of the progress through the phases of meta-analysis.

Despite the reasons for the large amount of I2 test discussed above, we investigate the source of heterogeneity with special methods. In the PROM-related portion, heterogeneity was moderate (I2 = 63%). Subgroup analysis based on test quality may reduce the amount of I2 in low quality studies. A closer look at the effect size anticipated in high-quality group studies showed that small-sample studies had the largest effect size (11).

When the relationship between fetal death and IHB was examined, the results of the analysis showed that IHB infection was not equal to a significant increase in the risk of fetal death in patients. It can be associated with pregnancy, premature delivery, high blood pressure, gestational diabetes or premature membrane rupture. However, other studies reject this effect and state that “fetal risk should not be increased to reduce the risk of placental infection”. In addition, the amount of I2 in this section showed low heterogeneity between studies. The forest map showed high heterogeneity in which OR studies were almost four to nine times higher than in other studies. These two studies have smaller examples than the other studies in this section (12).

In sections related to hypertensive disorders during pregnancy, including preeclampsia, eclampsia and gestational hypertension, IHD did not significantly affect these disorders during pregnancy. Studies confirming the possible effect of IHB on hypertensive disorders in pregnant women have shown that IHB-induced systemic inflammation is responsible for these effects (13). However, some unsuccessful studies believed that this effect can only be observed in some Asian studies, which did not pay attention to complex factors, such as higher viral load in the study group or the lack of gynecological and neonatal treatment in pregnant women (14). The result did not end in this part because the degree of heterogeneity was different in each part. The results of the preeclampsia and hepatitis study showed significant heterogeneity (I2 = 70%), so we conducted two subgroup analyzes depending on the quality and design of the study. The analysis of quality subgroups changed only the amount of I2 in the low-quality group (I2 = 30%), but the second analysis did not bring any effect.

High heterogeneity has been demonstrated by visual inspection of the forest plan, where OR studies are almost five times higher than in other studies. In this group, most of the work was done in Hong Kong, and one in Iran, so racial diversity can play a role in this heterogeneity (15). The last part of this study was devoted to postpartum hemorrhage and its possible association with inactive hepatitis B. The results of individual studies do not confirm this relationship. In three original studies, this effect was associated with the earlier occurrence of premature placenta and greater placental rupture in these pregnancies. The heterogeneity of study results was high, and quality-based subgroup analyzes changed in both groups.

Conclusion

Inactive HB infection status did not increase the risk of adverse events such as premature membrane rupture (PROM),
fetal death, preeclampsia, eclampsia, gestational hypertension, and prenatal bleeding during pregnancy. Women with IHB carriers can be treated like other low-risk pregnancies unless there are other prenatal complications, such as comorbidities during pregnancy or other related risk factors. However, these results should be evaluated in other well-designed studies.

Conflict of Interest: This study has no conflict of interest to declare by any author.

Disclosure: None

Human and Animal Rights: No rights violated.

References