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Observation of the effect of the pregnancy complicated with the hepatitis B infection on the lying-in women and neonates

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ABSTRACT

Objective: To investigate the effect of pregnancy complicated with the hepatitis B infection on the pregnancy outcome, immunological factors and the subgroup of lymphocytes in neonates.**Methods:** Subjects admitting to this hospital between January 1, 2016 and January 1, 2018 in this study were divided into two groups according to the hepatitis B infection, i.e. the observation group (infection) and the control group (healthy), with 60 subjects in each group. Pregnancy complications and the neonatal complications were all recorded, and furthermore, the subgroups of lymphocytes and the levels of immunoglobulin in the umbilical cord blood were measured.**Results:** The incidence rates of the premature rupture of fetal membranes, premature delivery, postpartum hemorrhage and pregnancy-induced hypertension syndrome in the observation group were all higher than those in the control group, and the differences had statistical significance. In the observation group, the incidence rates of the neonatal distress and asphyxia, and the levels of neonatal CD3⁺, CD4⁺, CD19⁺, IgA and IgM varied significantly from those in the control group, and the differences showed statistical significance. However, no significant differences were identified in comparison of the incidence rate of the cesarean delivery, neonatal deformity, neonatal death, or levels of neonatal CD8⁺ and IgG.**Conclusion:** During pregnancy, complications of hepatitis B infection results in the increases in the incidence rates of the premature rupture of fetal membranes and neonatal asphyxia, with influences on the levels of immunological factors and lymphocyte subgroups in the umbilical cord blood.© 2019 Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Complication of the hepatitis B virus infection in pregnancy, as the most common obstetrical infectious disease and also one of the high-risk pregnancies in the clinical practice, presents with a high incidence rate which is associated with the prevalence of hepatitis B in China, severely threatening the maternal and fetal health (Samadi et al., 2016; Zhao et al., 2017). According to the epidemi-

ological statistics, in China, over 130 million patients have been diagnosed with the hepatitis B infection or as the HbsAg carriers, with an incidence rate of hepatitis B infection in pregnancy ranging from 5.4% to 63.2% (Borchardt et al., 2016; Yin et al., 2017). Complication of hepatitis B virus infection in early pregnancy exacerbates the pregnancy reaction, and patients are more susceptible to the abortion in case of complication of acute hepatitis; in the late pregnancy, this complication usually causes an increase in other complications; during the delivery, due to the reduction in the synthesis of blood coagulation factor in liver, patients are also at a high risk of postpartum hemorrhage (Preiss and Sattar, 2008; Wong et al., 2009; Alberti et al., 2005). In addition, it also contributes to the higher risk of fetal distress, premature delivery and fetal death, severely threatening the health and life of mothers and babies, but there remain fewer studies focusing on the immunological status of neonates (Li et al., 2017). To further elaborate the effect of hepatitis b infection on the pregnancy outcome

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of the lying-in women, and the levels of neonatal immunological factors and lymphocyte subgroups, we selected a total of 120 lying-in women to compare the pregnancy outcome and neonatal indicators between the hepatitis B infection and non-infection, and the detailed information is reported as follows.

2. Material and methods

2.1. General data

A total of 120 subjects admitting to this hospital between January 1, 2016 and January 1, 2018 in this study were divided into two groups according to the hepatitis B infection, i.e. the observation group (infection) and the control group (healthy), with 60 subjects in each group. General data of the lying-in women and the neonates are shown in Table 1, and the data were comparable, with no significant differences ($P > 0.05$). In the observation group, 18 patients were diagnosed with the anomalies in ALT or AST.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) lying-in women for the first time of pregnancy and single pregnancy; (2) subjects in the observation group that were infected by the hepatitis B virus that conformed to the diagnostic criteria of hepatitis B virus infection through laboratory examination; (3) subjects reporting no other complications during pregnancy, and that had completed the pregnancy test and delivery; (4) subjects and their family that were informed of this study. This study had been approved by the Ethical Committee of the hospital. Exclusion criteria: (1) subjects complicated with other general fundamental diseases, like cardiac or pulmonary diseases; (2) subjects that had the hepatitis caused by infection of other viruses, or drug-induced hepatitis.

2.3. Protocols

Lying-in women with infection were isolated and received the symptomatic treatment, including the test and liver protection. Incidences of the pregnancy complications in lying-in women and neonates, and the measurements of the lymphocyte subgroups and immunological factors in neonatal umbilical cord blood were all recorded.

2.4. Observation indexes

2.4.1. Incidences of the pregnancy complications in lying-in women

We collected and compared the incidence rates of the pregnancy complications between the observation group and the control group, including the premature rupture of fetal membrane, premature delivery, postpartum hemorrhage and the ratio of caesarean section.

2.4.2. Incidences of the neonatal complications

Besides, we recorded and compared the incidences of the neonatal complications between two groups, including the fetal

distress, neonatal deformity, neonatal asphyxia and neonatal death.

2.4.3. Measurements of the lymphocyte subgroups in umbilical cord blood of neonates

We measured and compared the measurements of the lymphocyte subgroups in neonatal umbilical cord blood, including the levels of CD3⁺ T cells, CD4⁺ T cells, CD8⁺ T cells and CD19⁺ T cells.

2.4.4. Measurements of the immunoglobulins in the umbilical cord blood of neonates

We measured and compared the measurements of the immunoglobulins in neonatal umbilical cord blood, including the levels of IgA (immunoglobulin A), IgM (immunoglobulin M) and IgG (immunoglobulin G).

2.5. Statistical analysis

SPSS 19.0 software was applied in the statistical analysis. Age, gestational week, birth weight and the levels of the lymphocyte subgroups and immunoglobulins were recorded as the measurement data in normal distribution, expressed as means \pm standard deviation, and compared between two groups with the *t* test. Enumeration data, including the neonatal gender, delivery patterns and pregnancy complications, were compared between the two groups with the chi-square test. $P < 0.05$ suggested the statistical significance of difference.

3. Results

3.1. Incidence of the pregnancy complications in lying-in women

In the observation group, incidence rates of the premature rupture of fetal membranes (18.3%), premature delivery (11.7%), postpartum hemorrhage (20.0%) and pregnancy-induced hypertension syndrome (18.3%) were all higher than those in the control group (all $P < 0.05$). No statistical significance was identified in the difference of the incidence rates of caesarean section ($P > 0.05$; Table 2).

3.2. Incidence rate of the neonatal complications

In the observation group, the incidence rates of the fetal distress (8.3%) and neonatal asphyxia (11.7%) were all higher than those in the control group ($P < 0.05$), but no differences were detected in comparisons of the neonatal deformity and death between two groups ($P > 0.05$; Table 3).

3.3. Measurement of the lymphocyte subgroup in the neonatal umbilical cord blood

Significant differences were shown in comparisons of the CD3⁺, CD4⁺ and CD19⁺ levels in the neonatal umbilical cord blood between the two groups (all $P < 0.05$), but no difference was identified in the levels of CD8⁺ between two groups ($P > 0.05$; Table 4).

Table 1

Comparison of the clinical data of the lying-in women and neonates between two groups.

| Group | Age | Pregnancy weeks | Delivery | | Neonatal gender | | Neonatal weight |
|-------------------|------------------|------------------|-------------------|---------------|-----------------|--------|----------------------|
| | | | Caesarean section | Natural labor | Male | Female | |
| Control group | 25.61 \pm 2.64 | 38.52 \pm 0.60 | 32 | 28 | 27 | 33 | 3325.62 \pm 110.13 |
| Observation group | 26.02 \pm 3.13 | 38.40 \pm 0.69 | 29 | 31 | 26 | 24 | 3398.73 \pm 109.26 |
| <i>P</i> | 0.384 | 0.16 | 0.091 | | 0.084 | | 0.220 |

Table 2
Incidences of the pregnancy complications in the lying-in women [n (%)]

| Group | Premature rupture of fetal membrane | Premature delivery | Postpartum hemorrhage | Pregnancy hypertension | Caesarean section |
|-------------------|-------------------------------------|--------------------|-----------------------|------------------------|-------------------|
| Control group | 4(6.7) | 1(1.7) | 5(8.3) | 4(6.7) | 32(53.3) |
| Observation group | 11(18.3) | 7(11.7) | 12(20.0) | 11(18.3) | 29(48.3) |
| χ^2 | 10.472 | 13.522 | 12.846 | 10.472 | 2.032 |
| P | 0.001 | 0.000 | 0.000 | 0.001 | 0.154 |

Table 3
Incidences of the neonatal complications in two groups [n(%)]

| Group | Fetal distress | Neonatal asphyxia | Neonatal deformity |
|-------------------|----------------|-------------------|--------------------|
| Control group | 1(1.7) | 1(1.7) | 0(0.0) |
| Observation group | 5(8.3) | 7(11.7) | 1(1.7) |
| χ^2 | 11.162 | 11.697 | 1.042 |
| P | 0 | 0 | 0.312 |

3.4. Measurement of the immunoglobulins in the umbilical cord blood of neonates

In the observation, neonates had higher levels of IgA (0.41 ± 0.10) and IgM (0.64 ± 0.14) than their counterparts in the control group [IgA: (0.21 ± 0.06); IgM: (0.43 ± 0.10)], and the differences had statistical significance ($P < 0.05$). No significant difference was detected in comparison of the IgG level ($P > 0.05$; Table 5).

4. Discussion

Infection of hepatitis B virus in early pregnancy usually exacerbates and prolongs the pregnancy reactions, and makes the lying-in women more susceptible to the abortion than those with no infection (Hsu et al., 2012; Supriya et al., 2017). In the middle and later pregnancy, the massive production of hepatitis B viruses further dampens the cells, functions and synthetic capacity of liver, thereby altering the *in vivo* environment and functional stability of organs; thus, patients with infection are more vulnerable than those with no infection to the premature delivery, postpartum hemorrhage (Chen et al., 2016; Jinjuvadia and Liangpunsakul, 2014). Besides, hepatic dysfunction also affect the levels of albumin and synthesis of the coagulation factors, which gives rise to the entrance of humor into the tissue space, retention of water and sodium and the hypertension (Kumada et al., 2010; Vere et al., 2012; Wang et al., 2010). The higher incidence rates of premature rupture of fetal membrane, premature delivery, postpartum hemorrhage and pregnancy hypertension in the observation group than those in the control group, suggesting the effect of hepatitis B virus infection on the maternal health. In this study, despite that no statistical significance was identified in the difference of the ratio of caesarean section between two groups, caesarean section should be immediately considered in case of the moderate or heavy hepatitis, so as to avoid the complications like postpartum hemorrhage (Mokan et al., 2008; Stepanova et al., 2010).

Infection of hepatitis B virus during pregnancy can affect the growth and development of neonates mainly through the

Table 4
Measurement of the lymphocyte subgroup in the neonatal umbilical cord blood.

| Group | CD3 ⁺ | CD4 ⁺ | CD8 ⁺ | CD19 ⁺ |
|-------------------|------------------|------------------|------------------|-------------------|
| Control group | 42.52 ± 12.62 | 31.72 ± 12.07 | 27.51 ± 8.08 | 13.86 ± 5.20 |
| Observation group | 69.14 ± 9.72 | 45.70 ± 8.74 | 26.82 ± 9.11 | 9.22 ± 4.51 |
| t | 23.357 | 19.622 | 3.764 | 15.723 |
| P | 0.012 | 0.015 | 0.081 | 0.019 |

Table 5
Measurements of the levels of immunoglobulins in the umbilical cord blood in neonates (g/L, $\bar{x} \pm s$).

| Group | IgA | IgM | IgG |
|-------------------|-------------|-------------|-------------|
| Control group | 0.21 ± 0.06 | 0.43 ± 0.10 | 9.61 ± 2.23 |
| Observation group | 0.41 ± 0.10 | 0.64 ± 0.14 | 9.58 ± 2.34 |
| t | 11.024 | 10.537 | 1.258 |
| P | 0.027 | 0.029 | 0.213 |

mother-to-fetus transmission, and according to the epidemiological statistics in China, the incidence rate of mother to fetus transmission reaches 23.0–27.0%, severely influencing on the prevalence of the hepatitis B in children in China (Yang et al., 2017). Infection of hepatitis B virus in the pregnant women alters the intrauterine environment, the development and functions of the placenta and organs, and the intrauterine respiration pathway of fetus, thus resulting in the fetal distress, neonatal asphyxia and deformity (Janicko et al., 2013; Zheng et al., 2017). In the observation group, the incidence rates of fetal distress and neonatal asphyxia exceeded those in the control group. Although there was no statistically significant difference in the incidences of the neonatal deformity and death, hepatitis B virus infection remains to be the high-risk factor responsible for the neonatal deformity, which is associated with the alterations in the liver function and intrauterine environment, damage of the placenta and the direct teratogenic effect of hepatitis B virus (Chiang et al., 2013).

Umbilical cord blood is frequently adopted for evaluating the effect on the immunological status in neonates for the convenience in collection of the umbilical cord blood, and the abundant immune cells and immunological factors (Wang and Di, 2017). In this study, significant differences were found in the levels of CD3⁺, CD4⁺ and CD19⁺ in the neonates between two groups, revealing that the infection of hepatitis B virus alters the constitution of the immune cells in neonates and further the immune functions. IgM is lowly expressed without the stimuli of antigens, while the increase in IgM indicates the possibility of infection. Besides, significant differences were also shown in the levels of IgA and IgM between two groups, but no difference was found in the level of IgG. Thus, hepatitis B infection may affect the immunological factors and the lymphocyte subgroups in the neonatal umbilical cord blood, showing the significance in prediction of neonatal immunological functions and intrauterine infection.

5. Conclusion

In conclusion, during pregnancy, complications of hepatitis B infection results in the increases in the incidence rates of the

premature rupture of fetal membranes and neonatal asphyxia, with influences on the levels of immunological factors and lymphocyte subgroups in the umbilical cord blood.

Declaration of Competing Interest

There is no conflict of interest.

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Further reading

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