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AST to Platelet Ratio Index (APRI), Fib-4 Score, and Pregnancy Outcome of Pregnant Women with Hepatitis B

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Abstract

Hepatitis B virus infection in pregnancy has become a major concern in many developing countries. The relationship between hepatitis B virus infection and pregnancy is complex and puzzling. This study aimed to investigate the relationship between hepatitis B virus infection and pregnancy outcomes with the insights into the AST to Platelet Ratio Index (APRI) and Fib-4 score. This was a cross-sectional study on pregnant women with hepatitis B virus infections who underwent labor at dr. Zainal Abidin Hospital General Hospital, Aceh, Indonesia. Data were collected from the obstetric ward patient medical records from 2017 to 2019 and 77 pregnant women was identified to be infected with hepatitis B virus, of which 44 had complete medical record data and were included in the analysis. The median APRI in this study was 0.30 (0.1–1.2) while the median FIB-4 score was 0.74 (0.3-1.9). Delivery with live births was identified in 42 (95.5%) women. Term pregnancy and vaginal delivery were observed in 39 (88.6%) and 10 (22.7%) women, respectively, Complicated pregnancy was seen in 14 (31.8%) of pregnancies that included complications such as oligohydramnios, HELLP, severe preeclampsia, placenta previa, and premature rupture of membranes. APRI was higher in the stillbirth group (0.5 [0.2–0.8] p=0.682) and preterm birth group (0.4 [0.2–0.6], p=0.502). FIB-4 scores were higher in the stillbirth group (1.2 [0.5–1.8], p=0.517) and preterm birth group (0.9 [0.4–1.9], p=0.529). Hence, pregnancy does not always worsen liver function and is not related to the natural course of hepatitis B infection. Pregnancy with hepatitis B without fibrosis is not associated with poor pregnancy outcomes. Routine liver function examination is needed in pregnant mothers with hepatitis B virus infections.

Keywords: Fibrosis, hepatitis B, pregnancy

Introduction

Hepatitis B Virus (HBV) infection in pregnancy has become a serious issue that needs to be addressed in developing countries. HBV infection common signs include mild diarrhea, anorexia, nausea, vomiting, malaise, and abdominal pain in the gravid uterus. These signs are quite similar to pregnancy signs. Therefore, diagnosing HBV infection in pregnancy may be challenging. Women should receive hepatitis B surface antigen (HBsAg) at their first prenatal or trimester visits. Later, they should be tested again during pregnancy if necessary. Thus, for diagnosis purposes, the presence of HBsAg in the bloodstream remains the serological hallmark.[1,2]

Understanding the relationship between HBV infection and pregnancy is not easy. It is important to have a good analysis of maternal HBV infection impacts on pregnancy outcomes, particularly in the regions where the cases are prevalent. Even though most studies confirm pregnancy does not necessarily harm the function of the liver, other research suggests that it may affect the liver size and blood flow and be associated with significant gestational and fetal complications.[1,3–5]

In China, the prevalence of HBV infection among women of reproductive age may reach 2-8%, whereas it is only 0.4% in the USA. The majority of HBV-infected pregnant women are chronic carriers, as shown by a positive serum HBsAg status.[6] Prevalence of HBV infections in Indonesia was 0.2% in 2013 and 0.4% in 2018,

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while in Aceh, 0.7% in 2013 and 0.4% in 2018.[7]

While some studies suggest that maternal HBV infection, either symptomatic, asymptomatic, or cirrhosis, may be linked to unfavorable pregnancy outcomes like gestational diabetes, antepartum hemorrhage, birth abnormalities, stillbirths, and preterm delivery,[5,8,9] other studies agree that HBV infection during pregnancy is not linked to poor pregnancy outcomes similar to the general adult population.[1,10–12]

There have been noninvasive methods used to assess liver fibrosis in the past. A combination of two independent noninvasive tests, two or a blood test plus Elastography, can be employed. However, no single noninvasive test or model has been created yet to match the information gained from actual histology. An easy-to-use and accurate test for identifying severe fibrosis has been reviewed as the aspartate aminotransferase (AST) to platelet ratio index (APRI).[13] In individuals with chronic liver disease, an APRI score was first described in 2003. It was found to be positively connected with fibrosis..[9,13] APRI and fibrosis -4 (FIB-4) were positively correlated with the fibrosis score.[14]

Methods

This observational analytic study took place at Dr. Zainoel Abidin teaching hospital Banda Aceh, the major tertiary health institution in Aceh, within three years with a cross-sectional design. Data was taken from obstetric ward patients' medical records from 2017 to 2019. This study used a total sampling of all HbsAg-positive pregnant women who underwent delivery at RSUDZA in 2017-2019 and had complete data included in this study. Those with other co-infections were excluded, such as hepatitis C virus, HIV, TORCH, and Rubella.

Reactive HBsAg characterizes hepatitis B virus infection. The three primary outcomes of pregnancies were miscarriage (spontaneous abortion), preterm (<37w), or stillbirth (after 20 completed gestational weeks). Utilizing the method age (years) × AST [U/l]/ (platelets [10^9/l] × (ALT [U/l])1/2), The FIB-4 values were automatically computed. The formula [a]AST/ upper limit of normal]/ platelet count [10^9/L][o] × 100 was employed to calculate the APRI values.[14]

An independent t-test analyzed data to examine data with a normal distribution, whereas the Mann-Whitney test was employed to analyze not normally distributed data. This study was registered under number 1171012P and approved by the Ethics Committee for Health Research, Faculty of Medicine, Syiah Kuala University/ Dr. General Hospital. Zainoel Abidin Banda Aceh with number 76/EA/FK-RSUDZA/2019.

Result

In this research, 77 pregnant mothers were found with HBV infection but who have complete data and analyzed as many as 44 people.
The median APRI value was 0.30 (0.1-1.2), while FIB-4 was 0.74 (0.3–1.9). Delivery with live births was found in 42 (95.5%), with term pregnancy 39 (88.6%), vaginal delivery 10 (22.7%), and 14 (31.8%) of pregnancies experienced complications, such as oligohydramnios, HELLP, severe preeclampsia, placenta previa and premature rupture of membranes.

This study found 4.5% of stillbirths with serological markers similar to the live birth group. Age, AST, ALT, APRI, and Fib 4 in the stillbirth group were higher than the live birth group but not statistically different and still in the normal range. Haemoglobin and platelet

Table 1 Baseline Characteristic

Baseline Characteristic	Value
Age (years) (mean±SD)	31.27±5.419
Haemoglobin (g/dl) (mean±SD)	11.41±1.28
Platelet (.10^3/mm^3) (mean±SD)	265. 16±60.60
AST (g/dl) median (min-max)	23 (12–74)
ALT (g/dl) median (min-max)	13.50 (6–76)
APRI, median (min-max)	0.30 (0.1–1.2)
Fib 4, median (min-max)	0.74 (0.3–1.9)
Fetal Maturity n, %	
Preterm	5 (11.4)
Aterm	39 (88.6)
Mode of delivery n, %	
Vaginal Delivery	10 (22.7)
Sectio Caesaria	34 (77.3)
The outcome of pregnancy n, %	
Live birth	42 (95.5)
Stillbirth	2 (4.5)
Obstetric Complication n, %	
Placenta previa	1 (2.3)
HELLP	1 (2.3)
Oligohydramnios	2 (4.5)
Premature rupture of membranes	5 (11.4)
Severe preeclampsia	5 (11.4)
No complication	30 (68.2)

Table 2 Serological Marker Stratified by the Outcome of Pregnancy

	Live Birth (n=42)	Stillbirth (n=2)	P value
Age	31±5.4	37±2.9	0.127
Haemoglobin	11.4±1.3	11.2±1.3	0.855
Platelet	265±60.5	253±86.3	0.775
AST	23 (12–74)	31 (16–46)	0.888
ALT	13.5 (6–76)	18.5 (11–26)	0.821
APRI	0.3 (0.1–1.2)	0.5 (0.2–0.8)	0.682
Fib 4	0.7 (0.3–1.9)	1.2 (0.5–1.8)	0.517

Age, Hb, and platelet use the independent t-test. AST, ALT, APRI, and Fib 4 use the Mann-Whitney test

were lower than in the live birth group.

In this study, 11.4% of cases were found to be preterm. Haemoglobin in the preterm group was lower than in aterm pregnancies. Age, AST, ALT, APRI, and Fib 4 in the preterm group was higher than the aterm group but not statistically different and were still within the normal range.

Discussion

The study of Siakwa et al. observed that babies born from mothers with chronic HBV possess a higher risk for preterm delivery. The general effects of neonatal infections on birth outcomes have been one possible theory that underlies this risk. There has been a significant increase in pro-inflammatory cytokines among infected chronic HBV pregnant women. Several studies report that liver cirrhosis in pregnant women liver cirrhosis may be very harmful.[1]

It is unclear how chronic HBV infection affects pregnancy outcomes. When comparing HBsAg-positive women with controls, one sizable study found no changes in newborn weight, gestational age at delivery, the incidence of prematurity, neonatal jaundice, congenital abnormalities, or perinatal mortality. A relatively recent study, however, found a link between maternal HBV infection (HBsAg positive) and antepartum hemorrhage and gestational diabetes mellitus. There was a hypothesized connection to preterm birth.[15]

Scientific evidence of how chronic hepatitis B infections affect maternal pregnancy outcomes is not widely available. Whether or not the studies on this area of research are yet to be published or the presence of publication bias where studies that found insignificant relationships were not published is still unclear. Another explanation is that Scientists have yet to develop an interest in this area.[1]

Generally, women with chronic hepatitis B infections who are not suffering from advanced liver disease may tolerate pregnancy well. However, some patients show hepatitis signaling, and HBsAg-positive mothers should be monitored closely. Liver biochemical tests were obtained every three months during pregnancy and for six months postpartum. HBV-DNA testing is recommended concurrently or when there is an ALT increase.[15] Chronic hepatitis B without cirrhosis rarely causes problems during pregnancy.[16]

Table 3 Serological Marker Stratified by Fetal Maturity

	Preterm (n=5)	Aterm (n=39)	P value
Age	33.2±4.1	31.03±5.6	0.405
Haemoglobin	10.6±2.5	11.5±1.0	<0.001
Platelet	271±73.9	264±59.8	0.816
AST	35 (16–39)	23 (12–74)	0.159
ALT	18 (9–30)	13 (6–76)	0.616
APRI	0.4 (0.2–0.6)	0.3 (0.1–1.2)	0.502
Fib 4	0.9 (0.4–1.9)	0.7 (0.3–1.8)	0.529

Age, Hb, and platelet use the independent t-test. AST, ALT, APRI, Fib 4 use Mann Whitney test

Most cirrhosis-infected women who conceived achieved a successful pregnancy outcome. ALBI and APRI scores can predict pregnancy outcomes for women with chronic liver illness. Patient treatment in this group was enhanced by preconception counseling from a hepatologist or specialist obstetrician.[9]

In this study, we use a cut-off for significant fibrosis for APRI 1.5 with a specificity of 92% and sensitivity of 39%, and for Fib 4 3,25 with a specificity of 74% and sensitivity of 59%; all of the subjects in this study had no significant liver fibrosis. There is controversy over how hepatitis B affects pregnancy. Only a few studies have shown any adverse outcomes. Pregnancy itself does not affect the hepatitis B infection's natural course.

This research concludes that pregnancy with hepatitis B without fibrosis is not associated with poor pregnancy outcomes. A routine liver function examination is needed in pregnant mothers with hepatitis B virus infection to assess fibrosis. Interprofessional teamwork between internists, gastroenterologists, pediatricians, obstetricians, and midwives is essential in providing a holistic and integrated approach to pregnant women exposed to or who have viral hepatitis to prevent liver fibrosis and good pregnancy outcomes.

This study is paramount because it is the first research in Aceh with a high incidence of HBV infection. This study has limitations because we did not find hepatitis B patients with fibrosis, so we could not assess the pregnancy outcome in fibrosis patients.

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