THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 13 Issue 2

RESEARCH ARTICLE

PREDICTION OF OBSTETRIC COMPLICATIONS IN WOMEN WITH NEWLY DETECTED HEPATITIS A REPLICATIVE ACTIVITY

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OPEN ACCESS

PUBLISHED
28 February 2025

CITATION
Mitsoda, R. and Mitsoda, KM., 2025. PREDICTION OF OBSTETRIC COMPLICATIONS IN WOMEN WITH NEWLY DETECTED HEPATITIS A REPLICATIVE ACTIVITY. Medical Research Archives, [online] 13(2). https://doi.org/10.18103/mra.v13i2.6299

DOI
https://doi.org/10.18103/mra.v13i2.6299

ISSN
2375-1924

ABSTRACT

Resume. Prediction of obstetric complications in women with newly discovered hepatitis A repetitive activity. Mitsoda R. Mitsoda K-M.

A survey of 50 women who suffered from acute hepatitis A during pregnancy and their newborns and 100 somatically healthy women and their newborns. All women with newly identified hepatitis A pathogenic activity during pregnancy were divided into two groups: obstetric complications in childbirth and no pathological obstetric changes during the birth act. Based on the analysis of 54 factors, the 12 most significant factors were selected to predict the occurrence of obstetric complications in childbirth, specifically for women with newly diagnosed hepatitis A replicative activity during gestation. The probability of obstetric complications is statistically significant ($p < 0.05$) increasing as the level of risk increases. At the 1st level of risk, the likelihood of obstetric complications does not exceed 20.0%, whereas at the second level, it reaches 60.0% ($p < 0,05$).

Keywords: hepatitis, prognosis, complications, pregnancy, prevention.

Introduction

Despite advancements in medical science and the continuous adoption of innovative medical technologies aimed at controlling infectious diseases, viral hepatitis remains a major contributor to elevated rates of illness and mortality[1-5]. Hepatitis A /HA/ is an infection, which is vaccine-preventable, but there are 1.4 million new cases globally that occur annually[6]. The Hepatitis A vaccine (HA) is recommended for those at an increased risk of hepatitis A, including pregnant women who fall into the at-risk category[7]. The incidence of newly diagnosed HA infections is generally lower in high-income countries. In contrast, the rapid spread of the disease in low-income countries is often driven by poor hygiene, insufficient access to clean drinking water, and widespread malnutrition[8,9].

Hepatitis A is generally regarded as not being linked to severe outcomes or complications during pregnancy. Studies explore the clinical characteristics of acute hepatitis A virus (HAV) infection during pregnancy, finding a strong association between HAV infection in the second and third trimesters and an elevated risk of gestational complications and preterm labor[10]. Researchers have reported that more than half of the patients in the study group of pregnant women who experience acute hepatitis A infection during the second and third trimesters face gestational complications. These complications include premature contractions, placental abruption, and premature rupture of membranes, often resulting in preterm labor[11,12]. Studies have also highlighted severe acute liver injury associated with HAV in pregnant women, with one case requiring a living-donor liver transplantation during the second trimester[13].

At the same time, the development and implementation of new methods of prevention and treatment are always accompanied by several issues related to both the integral assessment of the effect of pharmaceuticals (or other means) on the main pathological process and accompanying complications.

The Aim

The goal is to monitor the course of pregnancy, childbirth, and the postpartum period in women who have recently shown hepatitis A replicative activity during pregnancy, as well as during the early neonatal period of their newborns, to predict and prevent obstetric complications.

Materials and Methods

Due to the low frequency of the studied pathologies in the population as a whole, and especially in pregnant women, a total observation method was used for 5 years. The inclusion criterion for a woman in our study was diagnosed with acute hepatitis A during the gestational process.

An analysis of the course of pregnancies in women who had acute viral hepatitis A (50 cases) during gestation and gave birth at the maternity hospital No. 4 in Kyiv and 100 pregnancies in women who gave birth in the physiological department of the maternity hospital in Uzhhorod was conducted. A developed study card was filled out for each case.

The diagnosis of hepatitis was established on the basis of anamnestic, epidemiological, clinical and laboratory data. A comprehensive laboratory examination included biochemical tests and detection of specific serological markers of viral hepatitis in the blood. In all cases, the diagnosis was confirmed by an infectious disease specialist.

In 36% of cases, women suffered from mild HAV and in 64% - moderate. Regarding the period of HAV incidence, up to 10 weeks of pregnancy, 8 cases were registered, from 11 to 20 weeks - 22; from 21 to 30 - 10 and also 10 cases in the gestation period from 31 to 40 weeks, 6 of them at the height of labor.

Groups of women are homogeneous in age, social status (women are married), to a certain extent specialty (housewives, or work in a profession not related to physical exertion and contact with teratogenic substances), live within the same time zone and conditions temperate continental climate.

In all subgroups, the significance level p>0.05 was achieved, as evidenced by numerical data: up to 20 years old – 21% in the control group and 18% in the comparison group (t=0.45); from 21 to 25 years old – 46% and 40% (t=0.71); 26-30 years old – 17% and 24% (t=0.99); 31-35 years old – 16% and 18% (t=0.29).

Statistical processing of the observation results was carried out using the Statystyka and Excel software packages. To calculate the prognostic significance of signs, the Student's criterion in the modification of N.M. Amosov and co-authors (1975) were used. This relatively simple approach assumes statistical independence of signs (symptoms and syndromes) that are used to describe the nature of the disease.

The essence of the methodology is to compare the frequency of an unfavorable result in patients with the investigated symptom (P1) with the average frequency of an unfavorable result in all patients examined for this indicator (P0). The corresponding mathematical value has the following form:

$$t = \frac{P_1 - P_0}{\sqrt{m_1^2 + m_0^2}}$$

where t is the "weight" of the feature (in points); m1 and m0 are average errors of P1 and P0 values.

By the formula, the parameter t was calculated for each symptom, and only positive characteristics of the prognostic importance of the symptom were taken into account (that is, only risk factors). For further use, those clinical signs were taken for which the values of the t criterion were greater than one. In the case of a small number of observations, insufficient for a statistically reliable conclusion, expert assessments were again used.

In the next stage, the relationship (correlation) of the selected parameters was checked. With a correlation coefficient of $r \geq 0.7$, two parameters were replaced by a generalized one or one of them was chosen to avoid overestimating the prognostic importance of a set of features. If $0.3 < r < 0.7$, then to reduce the error, attention was paid only to the extreme values of each of the indicators, compared with the possible value of the other. If $r < 0.3$, the parameters were considered uncorrelated.

The most significant indicators were combined into a risk map.

Experimental verification of the risk map was carried out based on three samples:

1) On the so-called "training" sample (observations with verified conclusions), which was used to assess the prognostic significance of clinical indicators;
2) The control sample, which also combined observations with verified conclusions, but which were not included in the training sample;
3) "Examination" selection of medical histories (the truth of the conclusions was checked by observations).

In the last stages, the dependence between the sum of points characterizing the condition of the patients and the probability of an adverse outcome was determined, as well as the degrees of risk were substantiated. The relationship between the sum of points, which characterizes the condition of patients, and the probability of an adverse outcome, as a rule, was non-linear and most often had an S-shaped character.

For an integral assessment of complications, complications of the gestational process, which are the most significant in the opinion of the obstetrician, were identified and systematized:

- during pregnancy – the threat of spontaneous miscarriage, the threat of late spontaneous miscarriage, the threat of premature birth, early toxicosis, gestational edema, preeclampsia, pyelonephritis, placental insufficiency, anemia, acute respiratory viral infections, drug addiction;
- during childbirth and the postpartum period – premature birth, delayed pregnancy, rapid childbirth, weakness of labor forces, the

inefficiency of labor induction, labor induction, labor augmentation, prenatal and early fusion of amniotic fluid, defect of the placenta and/or membranes, manual or instrumental revision of the uterine cavity, hypotonia, hyperthermia, anemia, postpartum endometritis, lochiometra, oligohydramnios and polyhydramnios, green or meconium amniotic fluid;

- regarding the condition of the fetus – antenatal death, asphyxia, cephalohematomas, clavicle fracture, acute ischemic damage of the central nervous system, hyporeflexia, respiratory disorders syndrome, cyanosis, intrauterine hypotrophy, prematurity, immaturity, hemolytic or conjugation jaundice, withdrawal syndrome and Erb's paresis.

Results

All pregnant women with the newly detected replicative activity of the hepatitis A pathogen were divided into two groups:

- with obstetric complications in childbirth;
- no pathological obstetric changes during the labor act.

Based on the analysis of 54 factors, 12 factors were selected that are most significant for predicting the occurrence of obstetric complications in labor for women with the newly detected replicative activity of HA during gestation. Moreover, factors that are easy to observe and accessible to a doctor even in an antenatal clinic were generally selected (Table 1):

Table 1. Prognostic significance of factors determining obstetric complications in labor in women with the newly detected replicative activity of the HA pathogen during pregnancy

№ n/n	Factor	Number of observations	Result			The average frequency of adverse results, %	Value, points
			Good	Unfavorable			
			persons	persons	%		
1	Increase in the level of aspartate aminotransferase up to three times increase	14	3	11	78,6	42,0	2,12
2	Increase in the level of bilirubin more than 100 μmol/l	8	1	7	87,5	42,0	2,05
3	Placental insufficiency	3	0	3	100,0	42,0	1,78
4	Mother's age up to 20 years	9	2	7	77,8	42,0	1,58
5	Threatened miscarriage	11	3	8	72,7	42,0	1,48
6	Gestational edema	2	0	2	100,0	42,0	1,44
7	Threatened preterm labor	5	1	4	80,0	42,0	1,23

8	Increased total bilirubin level up to 100 μmol/l	8	2	6	75,0	47,5	1,16
9	Increased alanine aminotransferase levels more than three times increase	7	2	5	71,4	42,0	1,16
10	Increased aspartate aminotransferase level more than three times increase	1	0	1	100,0	42,0	1,01
11	Chronic adnexitis in history	1	0	1	100,0	42,0	1,01
12	Hepatitis of moderate severity	15	6	9	60,0	42,0	1,0

Table 1 shows factors with positive values only, i.e. those that worsen the prognosis. The relatively small number of pregnant women with newly detected replicative activity of the HA pathogen is explained by its low frequency in the population, and even more so when combined with pregnancy. Some of the signs listed in the table were also rare. However, their clinical importance is not in doubt. The values of the listed signs in points were determined by heuristic evaluation.

Subsequently, during the course of the medical examination or for the purpose of short-term prognosis, indicators of prognostically important signs (scores) were added. Given the danger of incorrectly increasing the score due to the use of closely interrelated factors, the correlations between the selected clinical indicators were checked. It turned out that there was no significant relationship between them (in no case did the correlation coefficient exceed 0.3).

According to the results, a significant number of risk factors are consistent with the literature and mainly characterize the severity of hepatitis (increased alanine and aminotransferase levels, total bilirubin levels, and hepatitis severity) and pregnancy complications (placental insufficiency, threat of spontaneous miscarriage, gestational edema, and threat of premature birth).

For practical convenience, in the process of predicting the course of labor in pregnant women with the newly detected replicative activity of HA, four levels of probability of an unfavorable outcome were identified:

- Level I - the sum of points is less than 2.5;
- Level II - 2.5-5.0 points;
- Level III - 5.1-7.5 points;
- Level IV - > 7.5 points.

By adding the scores of each patient's signs, the total score was determined. The division of pregnant women depending on the score is shown in Table 2:

There was a statistically significant increase in the likelihood of adverse outcomes as the risk level increased (Fig. 1):

Table 2. Dependence of the probability of obstetric complications in pregnant women with newly detected HA replicative activity on the level of risk

Risk level	Total points	Number of observations	Result			Average theoretical frequency of adverse outcomes, %
			Favourable	Unfavorable		
				persons	%	
I	< 2,5	30	24	6	20,0	< 20,0
II	2,5-5	10	4	6	60,0	60,0
III	5,1-7,5	6	1	5	83,3	83,3
IV	> 7,5	4	0	4	100,0	100,0
Total		50	29	21	42,0	

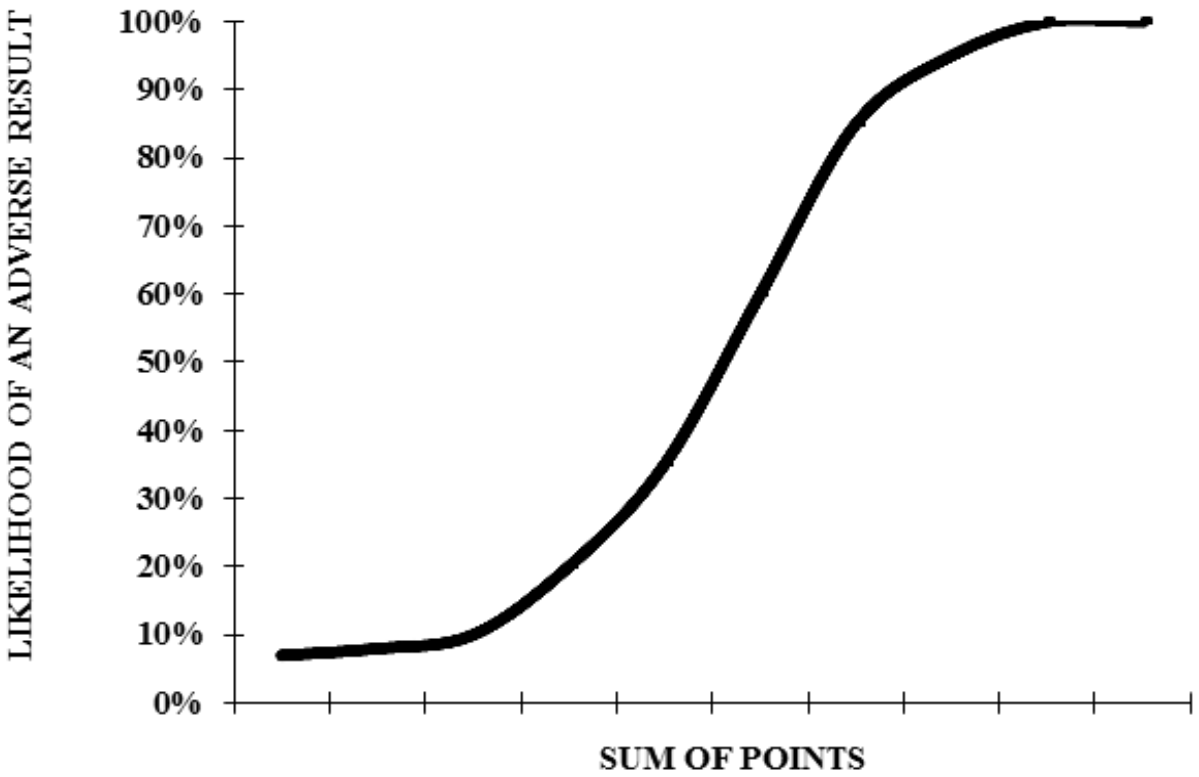

Fig. 1. General view of the dependence of the probability of an unfavorable outcome on the number of risk points.

Discussion

The results of the study are consistent with the data of other scientists that the combination of hepatitis with the gestational process leads to an increase in the frequency of complications[14-17].

However, the course of the gestational process in women who suffered from acute viral hepatitis A during pregnancy has not been studied sufficiently, since it is believed that the impact of hepatitis A on the course of pregnancy, childbirth, the postpartum period and the early neonatal period of their newborns.

The analysis of the gestational process in women who contracted acute viral hepatitis A during pregnancy showed that a significant number of risk factors are consistent with the literature and mainly characterize the severity of hepatitis (increased alanine and aminotransferase levels, total bilirubin levels, and hepatitis severity) and pregnancy complications (placental insufficiency, threat of spontaneous miscarriage, gestational edema, and threat of premature birth).

Therefore, it can be concluded that the probability of obstetric complications statistically significantly ($p<0.05$) increases with increasing risk. As can be seen from Table 2, at the first level of risk, the probability of obstetric complications does not exceed 20.0%, while at the second level it reaches 60.0% ($p<0.05$). Such a sharp increase in the likelihood of complications in childbirth in women with HA during pregnancy indicates the need to search for additional risk factors to ensure a smoother increase in the integrated risk of complications. On the other hand, it can be argued that the definition of the second, and even more so the third or fourth level of risk requires the mandatory use of preventive measures in the system of medical care for women with HA.

Conclusions

According to the results obtained, the main complications during the gestational process in women with acute hepatitis A during pregnancy are the following pregnancy complications - placental insufficiency, the threat of spontaneous miscarriage, gestational edema, and the threat of premature birth, the occurrence of which is mainly due to the severity of viral hepatitis.

Conflict of Interest:

None

Acknowledgements:

None

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