

## FUNCTIONAL STATE OF THE LIVER IN PREGNANT WOMEN WITH PNEUMONIA

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### Resume

**Relevance.** Analysis of the causes of maternal mortality in pregnant women with extra-hospital pneumonia and monitoring of the course and outcome of pregnancy in women with acute respiratory viral infection and pneumonia showed the development of hepatic cell insufficiency (LCI) in some patients. Severe impairment of liver function with development of encephalopathy and coagulopathic bleeding and polyorgan failure has resulted in high maternal and perinatal mortality rates.

**Description of Clinical Observation.** A prospective observational study - the course and outcome of pregnancy in women with acute hepatic-cell insufficiency against the background of acute respiratory viral infection and pneumonia - was conducted. The sample included 78 pregnant women with signs of liver dysfunction and jaundice. Previous ODS and pneumonia was also included as criteria. The exclusion criteria were another concomitant pathology. The study was conducted in the city Perinatal Center № 1 and in the Regional Perinatal Center of Bukhara. The study period is 2014-2017.

**Conclusion.** The results of the analysis of the course and outcome of pregnancy in women with PCN developing against the background of extra-hospital pneumonia indicate a burdened course of gestational process. The catastrophic situation is due to the high risk of coagulopathic bleeding associated with a double hemostasis disorder. On the one hand, violations of blood-clotting factors and on the other hand, expressed by coagulopathies. Due to the progression of DHS, disorders in the microcirculation system, and perfusion of vital organs, polyorganic insufficiency and disorders in uterine and placental perfusion cause the development of perinatal complications of hypoxic genesis.

**Keywords.** Liver function, pregnancy, hepatic cell failure, complications of acute respiratory viral infection and pneumonia

**Introduction.** In recent years there has been an increase in the number of pregnant women with acute respiratory viral infection (ARVI) and pneumonia and hepatic-cell insufficiency [1,2,3]. According to modern data, the outcome of pregnancy and childbirth in women with pneumonia against the background of acute respiratory viral infection largely depends on the compensatory and adaptive responses of organs and systems, the severity of respiratory insufficiency, the presence of obstetric complications, the functional state of the liver and the hemostasis system [4-6]. Accompanying hepatic-cell insufficiency worsens the prognosis and may lead to development of extreme conditions requiring urgent measures, which in its turn promotes progression of polyorganic insufficiency and lethal outcome [8-10]. This fact has induced us to analyze the course and outcome of pregnancy in women with acute PCN against the background of ODS and pneumonia.

Description of clinical observation. A prospective observational study was conducted. The sample included 78 pregnant women with signs of liver dysfunction and jaundice. The criteria for inclusion were also: previous ARVI, pneumonia. The exclusion criteria were another concomitant pathology. The study was conducted in the city Perinatal Center № 1 and in the Regional Perinatal Center of Bukhara. Period of the study 2014-2017.

In terms of timing, 6 (7.7%) of pregnant women were under 12 weeks, 8 (10.3%) were under 14-20 weeks, 53 (67.9%) were under 22-28 weeks, and 11 (14.1%) were under 32-38 weeks. All patients reported ODS prior to jaundice. Terms of jaundice development after acute respiratory viral respiratory infections in 12 patients were 6-7 days, in 3-10-12 days and in 28 patients - more than 2 weeks.

The results of the analysis show that at PCN the terms of jaundice occurrence coincide with 22-28 weeks of 53 (67,9%). Analysis of anamnesistical data suggests that many symptoms indicating liver dysfunction were present much earlier than the appearance of jaundice staining of skin and mucous membranes.

The results of clinical symptom analysis in pregnant women with PCN showed hypothermia in 8 (10.3%). Hypothermia development was preceded by fever for 4.5 days (SD=1.2), then normalization of temperature was observed. In the vast majority of pregnant women during the period of jaundice body temperature was within 37-38°C, on average 37.50°C (SD=1.8) and 11 (14.1%) had febrile temperature. It should be noted that an increase in body temperature was observed during the period of ODS to the febrilic numbers, then there was a period of decline and on average for 7.7 (SD = 1.3) days there was a new wave of body temperature rise. All patients noted progressive weakness, general disruption, rapid fatigue. Headache was a characteristic feature, severe during the ODS period, then periodically increasing during the day, disturbed by reduced and/or no appetite, dry mouth and thirst.

Nausea and/or nausea of a permanent nature, burp was also noted in an overwhelming number of pregnant women (83.3%). At the onset of jaundice staining, increased irritability, anxiety, agitation were observed, followed by apathy, lethargy and some retardation. Against the background of deterioration of general condition in 43 (55.1%) pregnant women vomiting 2-3 times per day of "coffee grounds" color was observed. 29 (37.3%) pregnant women complained of constipation and discoloration of feces. It was objectively noted: tongue was covered, dry in 69 (88.5%), itching in 4 (5.1%) pregnant women.

There were signs of increasing respiratory insufficiency in the intensive care unit. Pregnant women noted pain in the heart area, difficulty breathing, shortness of breath at rest. Attention was drawn to the increase in the number of heart beats on average at the time of primary consultation to 96.8 (SD = 7.6) beats per minute. Then there was a decrease in heart rate and on average reached 78.4 (SD=7.2) beats per minute. In this case, 19 (24.4%) of tachycardia was replaced by pronounced bradycardia. With regard to AD, the majority of pregnant women had normotension at the initial examination, followed by hypotension, and in 19 (24.4%) pregnant women AD reached 90/60, averaging 4 hours later. ADH averaged 90.6 (SD=5.8) mmHg, DAD 68.4 (SD=4.8) mmHg. Diffuse changes in myocardium, ischemia were recorded on the ECG. Extracystolia in 43 (55.1%) pregnant women.

The results of peripheral blood tests show a decrease in the number of erythrocytes from  $3.2 \cdot 10^{10}$  (SD=0.4) at intake to  $2.2 \cdot 10^{10}$  (SD=0.6) before delivery. Along with a decrease in erythrocyte levels observed a decrease in hemoglobin from 102 g / l (SD = 5.8) before delivery to 80.4 (SD = 6.2). There was a moderate leukocytosis of  $10.7 \cdot 10^9$  (SD=2.5), before delivery resolution there was a significant reduction to an average of  $5.2 \cdot 10^9$  (SD=2.8) ( $p < 0.01$ ). The results of the analysis

indicate the shift of the leukocyte formula to the left, the number of neutrophil wand nuclei increased and by the time of delivery it reached 58.4% on average (SD=6.2). Attention is drawn to the progressing lymphopenia with 18.7% (SD = 2.0) at admission to 8.5% (SD = 2.1) before delivery (p<0,01). There is some acceleration of SCE. As for the hematocrit, the average rate at entry was 28.8% (SD=2.8), declining progressively, and before the termination of pregnancy was 16.8% (SD=2.4) (p<0.01).

The results of these studies indicate a progressive reduction in protein levels, which before delivery were on average 45.5 (SD = 0.4), while at intake was 59.7 m / l (SD = 1.4). The growth of total bilirubin to 90.7  $\mu$ mol/l was mainly due to direct fractions with insignificant activity of liver enzymes. As follows from the data in Table 1, hypoglycemic tendencies were observed.

**Table No. 1**

**Dynamics of blood chemistry indicators and hemostasis system in pregnant women with PCN**

Parameters to be studied	Reference Group n=30	Периоды наблюдения		
		Upon admission	Via . 2 hours	Through 6 o'clock
Total protein, g/l	65,8±3,2	59,7±1,4	52,8±1,5	45,5±0,4
Glucose, moth. /l	4,4±0,2	4,1±0,3	3,9±0,2	3,0±0,5
Urea, moth. /l	2,1±0,3	2,7±0,2	3,5±0,3	4,0±1,1
АЛТ, E/l	30,9±2,5	45,7±3,1	48,7±3,7	48,7±4,1
ACT, E/l	29,4±1,8	33,5±2,6	37,8±2,4	39,8±3,1
Bilirubin, $\mu$ mol/l. -General -not straight -directly	8,4±2,1 5,5±0,6 2,9±0,1	50,7±4,2 20,0±2,1 30,7±3,5	67,8±4,3 20,1±2,6 47,7±3,7	90,7±11,2 31,3±3,5 59,4±4,8
Thrombocyte count, *10/ l	264,0±18,2	220,0±13,5	170,4±13,1	150,8±12,3
Fibrinogen, g/l	3,0±0,5	5,2±2,1	3,7±0,3	2,0±0,2
AЧТВ, c	30,4±3,6	28,5±2,5	25,8±2,9	23,7±3,8
Prothrombin time	14,4±2,9	22,4±2,2	28,0±3,5	30,1±4,1
Protein C, %	120,0±15,9	94,5±18,3	80,4±11,9	72,4±5,0
AT III, %	89,4±5,7	80,5±12,7	77,4±9,5	70,5±4,9

The results of the analysis of hemostasis system indices in pregnant women with transferred ARVI, complicated by pneumonia and PCN development, testify to the progressive decrease of platelet level, as far as fibrinogen concentration is concerned, hyperfibrinogenemia was observed at the primary examination, and then fibrinogen content was progressively decreased. As it follows from the data of the table the progressive deterioration of both ACTV and PI was noted, which also indicates the consumption of blood clotting factors and the depletion of the most important anticoagulants. Thus, the content of ATP III authentically decreased before pregnancy termination (p<0,01) and the dynamics of protein C decrease was also significant (p<0,01).

Progressive hypovolemia contributed to the deterioration of organ hemodynamics of vital organs and liver functions and to the progression of PCN. Hemostasis system violation has a complex genesis in this case, double hemostasis disturbance is observed. On the one hand, there is a disturbance in the synthesis of clotting factors and the most important physiological anticoagulants (antithrombin (AT) III, protein C). On the other hand, the consumption of clotting factors is increasing, due to the presence of an inflammatory focus (pneumonia), which leads to depletion of anticoagulants, and the risk of coagulopathic bleeding increases (Table 2).

**Table #2**

**Results of differentiated analysis of hemostasis parameters in pregnant women with PCN**

Parameters to be studied	Number of people surveyed , N=78
	Absolute number, %
Total protein, g/l	
-< 50	52(66,7%)
-< 40	26(33,3%)
Bilirubin total, mmole/l.	
-≥ 100	58(74,4%)
-< 100	20(25,6%)
Thrombocyte count	
-< 200	45(57,7%)
-< 150	33(42,3%)
Fibrinogen, g/l	
-<4,5	30(38,5%)
-< 3,0	28(35,9%)
-< 2,0	20(25,6%)
Protein C	
-< 80	52(66,7%)
-< 70	26(33,3%)
AT III	
-< 80	52(66,7%)
-< 70	26(33,3%)

As it follows from the data in Table 2, against the background of the therapy there is a steady decrease in the level of both blood-clotting factors and the most important physiological anticoagulants against the background of PCN progression. A catastrophic reduction of protein (to values below 40.0 g/l in 33.3% of pregnant women) and thrombocytes in 43.3% below 150\*10<sup>9</sup>/l has been noted. The increase of bilirubin level mainly due to direct fractions on the background of insignificant activity of transaminases can be used as markers of liver damage.

The main principles of observation and treatment of pregnant women with developed PCN were:

1) Protein restriction, exclusion of proteins in the diet of animal origin with priority on proteins of plant origin.

Oral hydration in the amount of 150-200 ml per hour.

3. infusion therapy with physiological solutions, under diuresis control.

4. Appointment of lactulose in the amount of 30 ml - 3 times per day.

5. Elimination of administration of protein preparations (SPP, albumin).

6. Siphon enemas

7. Termination of pregnancy.

We have approached the question of the need to terminate the pregnancy, the method of delivery and the scope of surgical interventions in stages. Against the background of treatment, dynamic control made it possible to form groups of patients:

- Group I consisted of 30 pregnant women, who had an increase in the level of total bilirubin to 100 g/l on average, mainly due to direct fractions, a decrease in the concentration of total protein to an average of 50.0 g/l and the level of platelets to 150 on average. There was an expressed consumption of blood clotting factors (fibrinogen up to 4.0 g/l on average). As for the level of physiological anticoagulants, the content of ATP III decreased to 70, protein C to 80.
- Group II consisted of 20 patients whose laboratory test parameters were without positive dynamics, but there was no deterioration of both well-being and laboratory test parameters.
- Group III consisted of 28 pregnant women, in whom positive dynamics were registered. Along with the improvement of well-being there was a decrease in total bilirubin and liver enzymes, an increase in platelet count, total protein level, blood clotting factors and physiological anticoagulants.

At detection of signs of hourly growth of total bilirubin, increase of intoxication the question of delivery in pregnant women was raised. The question about the method of delivery was solved taking into account the condition of the pregnant woman, the preparedness of the birth tracts and the indicators of hemostasis system. At unpreparedness of birth ways the method of choice was caesarian section.

**Table 3**  
**Outcome of pregnancy in women with PCN**

The outcome of pregnancy	Gestation period	Total protein, g/l	Total bilirubin	Thrombocyte count	AT III	Protein C
Caesarean section, n=28	32,4	42,2±2,5	120,4±9,2	135,8±8,1	76,8±3,2	78,4±3,4
Uterine amputation without appendages, n=3	34,6	40,4±1,9	127,0±8,7	125,4±7,3	74,5±2,6	70,8±2,9
Uterine extirpation without appendages, n=2	35,8	37,7±1,6	130,5±5,6	110,9±5,2	67,5±1,5	70,4±1,9
B-Lynch stitches, n=5	36,4	44,4±2,4	100,5±8,2	127,0±6,1	70,4±1,6	79,5±4,3
Prolongation of pregnancy, n=50	36,8	50,5±3,1	26,4±1,2	198,5±9,1	85,0±5,1	110,4±8,2

With pronounced coagulopathy of consumption and progressive thrombocytopenia (<110.9 SD=5.2), and critical indicators of AT III <67.5 and protein C, the volume of surgery was expanded to amputation and uterine extirpation without appendages.

In women, against the background of the developed PCN, the average mass of newborns was significantly lower than that of the control group 3124.7 g. (SD=19.5) compared to 2254.6 g. in the control group. (SD=10.8) in the main group on the Apgar scale at the first minute showed that the highest number of children with a score of 4-5 was recorded in women in the main group and was 34.6% compared to 6.7% in the control group ( $p < 0.01$ ). The results of the newborn assessment after 5 minutes showed that the number of children with a score of 8-10 in women with PCN continued to be twice as high (6.4% vs. 3.3% in the control group).

**Conclusion.** The results of the analysis of the course and outcome of pregnancy in women with PCN developing against the background of extra-hospital pneumonia indicate a burdened course of gestational process. The catastrophic situation is due to the high risk of coagulopathic bleeding associated with a double hemostasis disorder. On the one hand, violations of blood-clotting factors and on the other hand, expressed coagulopathies. Due to the progression of DVS syndrome, disorders in the microcirculation system, and perfusion of vital organs polyorganic insufficiency and disorders in uterine and placental perfusion cause the development of perinatal complications of hypoxic genesis.

#### **Authorship**

- The concept and design of the study– N.S. Nadirkhanova, M.M. Asatova
- Collection and processing of material– N.S. Nadirkhanova
- Statistical data processing– N.S. Nadirkhanova
- Writing a text– M.M. Asatov
- Editing - N.S. Nadirkhanova

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