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Changes in Laboratory Parameters in Patients with Acute Calculous Cholecystitis Amid Full–Scale War in Ukraine

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Abstract

Objective. To investigate changes in laboratory parameters in patients with acute calculous cholecystitis during full–scale war in Ukraine.

Materials and Methods. We examined complete blood counts, coagulograms, biochemical markers of liver and kidney function, lipid profiles, and levels of D–dimer, C–reactive protein, cortisol, ferritin, procalcitonin, magnesium, and vitamin D levels in 78 patients with acute calculous cholecystitis who were treated at the Odesa Regional Clinical Hospital between 2022 and 2025 (prospective group), and in 72 patients with acute calculous cholecystitis who were treated in the Department of General and Minimally Invasive Surgery at the Odesa Regional Clinical Hospital from 2017 to 2021 (retrospective group).

Results. The values for erythrocyte sedimentation rate, platelet count, white blood cell count, monocyte count, prothrombin time, prothrombin index, and levels of fibrinogen, glucose, bilirubin, total cholesterol, creatinine, low–density lipoproteins, cortisol, D–dimer, procalcitonin, and activated partial thromboplastin time in the prospective group were statistically significantly higher than the corresponding values in the retrospective group, while the values for red blood cell count, lymphocyte count, hemoglobin levels, hematocrit, international normalized ratio, blood fibrinolytic activity, total protein, ferritin, magnesium, and vitamin D were statistically significantly ($p < 0.001$) lower than in the retrospective group.

Conclusions. Due to the hostilities in Ukraine, the etiopathogenic mechanisms and clinical and laboratory characteristics of acute calculous cholecystitis are changing; this condition occurs against a background of impaired function of the digestive, hepatopancreatobiliary, and urinary systems, changes in patients' immunological status with increased severity of inflammatory processes, alterations in the blood coagulation system, and the development of anemia. Studying changes in laboratory parameters resulting from disturbances in the compensatory and adaptive mechanisms in patients with acute calculous cholecystitis during the period of full–scale war in Ukraine is necessary to determine diagnostic and therapeutic strategies, which include both conservative and surgical treatment methods.

Keywords: laboratory parameters; acute calculous cholecystitis; war in Ukraine.

The number of patients with acute calculous cholecystitis (ACC) during the period of military operations in Ukraine has increased compared to peacetime, accounting for up to 10% of patients with urgent abdominal pathology and 10–15% of the adult population, and the course of the disease itself exhibits certain clinical features [1–3].

Constant shelling of civilian homes intensifies pathological emotional processes, stress and act as factors that may support the neurogenic and psychogenic theories of the onset and development of ACC , the provision of medical care to civilian patients with ACC and the treatment of wounded individuals in accordance with evacuation protocols, transported from the front lines have altered the course of life under martial law [4–6]. Furthermore, the etiopathogenic mechanisms and clinical and laboratory characteristics of ACC [1, 3, 6] are altered due to dysfunction of the digestive and hepatopancreatobiliary systems, changes in immunological status, blood coagulation system abnormalities, and anemia in patients [7–9].

Blood stasis in the vascular system and gallbladder distension with increased intravesicular pressure due to impaired bile outflow, followed by the development of inflammatory and destructive changes in the organ wall and throughout the body, are characteristic features of the course of ACC during wartime [9–11].

Stressful conditions caused by constant shelling, explosions, sleep deprivation, a high–calorie diet rich in carbohydrates and fats, excessive alcohol consumption, and smoking lead to metabolic disturbances, as evidenced by changes in clinical and laboratory parameters; these should be regarded as triggers for the development of ACC during wartime [12–14].

The multimodal stress response is a complex, multilevel process through which the body reacts to a threat or stressor by simultaneously activating physical, psychological, behavioral, and biochemical mechanisms.

The main components of the multimodal stress response are as follows.

Neuroendocrine changes: activation of the hypothalamic–pituitary–adrenal axis, in which the hypothalamus, pituitary gland, and adrenal glands trigger the release of cortisol.

Activation of the sympathetic–adrenal system: rapid release of catecholamines (adrenaline and norepinephrine).

Increased levels of stress hormones–cortisol, epinephrine, and glucagon–which lead to elevated blood sugar levels.

Metabolic changes: a shift in metabolism to provide energy to vital organs.

Catabolism: the breakdown of proteins and fats to meet energy needs.

Immunological changes: activation of inflammatory processes and the release of cytokines, which are necessary for wound healing but can be harmful if produced in excess.

Psycho–emotional/behavioral component: the "fight–or–flight" response.

Cognitive impairment, irritability, and insomnia may occur [12, 14].

Metabolic processes occur with the direct involvement of connective tissue metabolism, taking into account the connective tissue basis of the vascular endothelium, macro– and trace elements (calcium, magnesium), the varying degrees of activity of redox processes involving iron, zinc, enzymes, B vitamins (including folates), and vitamin D [15, 16].

Thus, the study of laboratory parameters for the diagnosis and selection of treatment methods for ACC in the context of full–scale war in Ukraine is a pressing issue.

Objective of the study: to investigate changes in laboratory parameters in ACC under conditions of full–scale war in Ukraine.

Materials and Methods

Study design. A cohort–based, prospective–retrospective, single–center study with elements of comparative analysis was conducted.

Patient selection was based on the clinical severity of ACC (stages I, II, III), in accordance with the international Tokyo Guidelines (Tokyo Guidelines 2018 – TG18), in accordance with which the proposed treatment strategy–laparoscopic cholecystectomy using the standard technique–was applied [17, 18].

The prospective part of the study was based on clinical data from 78 patients with ACC who were treated at the Odesa Regional Clinical Hospital between 2022 and 2025 (prospective group). There were 59 women (75.6%) and 19 men (24.4%).

The retrospective analysis included the medical records of 72 patients with ACC who were treated in the Department of General and Minimally Invasive Surgery at the Odesa Regional Clinical Hospital between 2017 and 2021 (retrospective group). There were 43 women (59.7%) and 29 men (40.3%).

Inclusion criteria for patients in the study: ACC, age 18 to 82 years, provision of voluntary informed consent to participate in the study (applies to patients enrolled in the prospective part of the study). Exclusion criteria for patients in the study: critical condition with unstable hemodynamics; history of cancer; severe comorbidities with organ dysfunction; refusal to participate in the study (applies to patients enrolled in the prospective part of the study) [17, 18].

Ultrasound examination (US) of the abdominal organs is considered the primary method in the modern diagnostic algorithm for ACC [19].

The extent of destructive changes was assessed based on the results of a pathological examination of the resected gallbladders [20].

An analysis of laboratory data from patients with ACC during the preoperative evaluation period was conducted. A quantitative and qualitative complete blood count characterized the state of the hematopoietic system and the main functions of the blood, and made it possible to determine the presence of a pathological process in the body. The following parameters were studied using standard methods: red blood cell count, hemoglobin and hematocrit levels, erythrocyte sedimentation rate (ESR), as well as lymphocyte and monocyte counts and blood coagulation parameters: platelet count, prothrombin time (PT), prothrombin index (PI), international normalized ratio (INR), activated partial thromboplastin time (APTT), fibrinogen level, and fibrinolytic activity of the blood (FLAK) [21–23].

The following were analyzed: total protein, glucose, and total bilirubin levels in the blood; liver and kidney function tests: lactate dehydrogenase (LDH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) activity; creatinine levels, and lipid metabolism markers: cholesterol, low–density lipoproteins (LDL), D–dimer, and C–reactive protein (CRP).

We determined the levels of cortisol (a stress hormone) in serum and 24–hour urine, as well as levels of ferritin, procalcitonin, magnesium, and total vitamin D [24].

Statistical Analysis. SPSS version 26.0 was used for statistical analysis. Quantitative measures are presented as the mean (M) and standard deviation (SD). To compare quantitative indicators between groups, the Student's t–test (for normally distributed data) was used, with a 95% confidence interval (95% CI) for the mean. Differences were considered statistically significant if the p–value was less than 0.05.

To determine the extent of the impact of wartime on the laboratory parameters under study in the compared groups,

the odds ratio (OR) was calculated; it indicates by how many times the parameter under study in the prospective group of patients with ACC differs from the corresponding parameter in the retrospective group of patients with ACC.

The OR was calculated using the following formula: OR = (A/B) : (C/D), where A is the absolute value; B is the mean reference value of the laboratory parameter of interest in the retrospective group of patients with ACC; C is the absolute value, and D is the mean reference value of the parameter of interest in the prospective group of patients with ACC. The OR values were interpreted as follows.

HR = 1: the odds of the event occurring are the same in both groups; the factor has no effect (no association).

OR > 1: the odds of the event occurring are higher in the prospective group than in the retrospective group; the factor carries a risk.

OR < 1: the probability of the event occurring is lower in the prospective group than in the retrospective group; the factor does not carry a risk [20, 21].

Results

The mean age of patients in the prospective group was (45.7 ± 0.5) years, and in the retrospective group, (65.3 ± 0.5) years, which was 1.4 times higher. Thus, a higher average age is characteristic of patients with ACC during peacetime .

During wartime, ACC was diagnosed 3.1 times more frequently in women than in men; during peacetime, it was diagnosed 1.5 times more frequently in women. Thus, the incidence of ACC in women increased 2.1–fold during wartime compared to peacetime.

In the prospective group, the incidence of Grade I ACC was 1.2 times lower, Grade II ACC was 2.4 times higher, and Grade III ACC was 2.2 times higher than in the retrospective group.

Destructive forms of gallbladder inflammation (phlegmonous, gangrenous) associated with ACC were detected in 62 (79.5%) patients in the prospective group and in 33 (45.8%) patients in the retrospective group, which was 1.9 times less common ($p < 0.05$). Catarrhal ACC was detected in 16 (20.5%) patients in the prospective group and in 39 (54.2%) patients in the retrospective group, which was 2.4 times more common ($p < 0.05$).

Laboratory test results are of fundamental importance for confirming the diagnosis of ACC, identifying the characteristics of its course, monitoring its progression, and determining the management algorithm for this category of patients (*Table 1*).

Analysis of the study results revealed statistically significant ($p < 0.001$) differences in the indicators between the prospective and retrospective groups. In the prospective group of patients with ACC, ESR levels were significantly

Table 1. **Complete blood count parameters in patients with CHD (M ± SD)**

Parameter	Reference value		Patient group				p	
			Retrospective (n = 72)		Prospective (n = 78)			
	h	f	m (n=29)	f (n=43)	m (n=19)	g (n=59)	p_1 (h)	p_2 (f)
Red blood cells, $\times^{10^{12}}$	4.0–5.0	3.7–4.7	4.9 ± 0.2 95% CI (4.97, 4.92)	4.76 ± 0.24 95% CI (4.8, 4.72)	3.50 ± 0.16 95% CI (3.58, 3.42) OR = 1.35	3.40 ± 0.15 95% CI (3.44, 3.36) OR = 1.38	< 0.001	< 0.001
Hemoglobin, g/L	130–160	120–140	161.6 ± 6.5 95% CI (164.5, 158.7)	140 ± 6.0 95% CI (140.9, 139.1)	101.0 ± 5.3* 95% CI (102.2, 99.8) OR = 1.59	100.0±5.2* 95% CI (100.7, 99.3) OR= 1.41	< 0.001	< 0.001
Hematocrit, %	35–54		54.4 ± 2.2 95% CI (55.2, 53.6)	52.7 ± 2.3 95% CI (53.4, 52.0)	34.0 ± 1.6* 95% CI (34.7, 33.3) OR = 1.6	35.1 ± 1.7* 95% CI (35.52, 34.8) OR= 1.51	< 0.001	< 0.001
White blood cells, $\times 10^9$/L	4.0–9.0		9.25 ± 0.46 95% CI (9.42, 9.08)	10.4 ± 0.52 95% CI (10.55, 10.25)	11.1 ± 0.48* 95% CI (11.31, 10.89) OR = 0.83	12.5 ± 0.48* 95% CI (12.62, 12.38) OR = 0.84	= 0.008	= 0.004
Lymphocytes, %	19–37		36.4 ± 0.95 95% CI (36.78, 36.01)	37.2 ± 1.8 95% CI (37.73, 36.7)	13 ± 0.65* 95% CI (13.29, 12.7) OR = 2.8	12 ± 0.61* 95% CI (12.16, 11.84) OR = 3.1	< 0.001	< 0.001
Monocytes, %	3–10		14.2 ± 0.61 95% CI (14.42, 13.98)	12.1 ± 0.5 95% CI (12.25, 11.95)	17 ± 0.84* 95% CI (17.38, 16.62) OR = 0.8	17 ± 0.85* 95% CI (17.22, 16.78) OR = 0.7	= 0.021	= 0.018
ESR mm/h	1.0–10.0	2–15	10.1 ± 0.51 95% CI (11.29, 8.91)	15.5 ± 0.78 95% CI (15.73, 15.27)	16.1 ± 0.86* 95% CI (16.48, 15.72) OR = 0.63	17.1 ± 0.86* 95% CI (17.32, 16.88) OR = 0.91	< 0.001	< 0.001

Note. * – $p < 0.001$ compared to the corresponding retrospective data by gender; M – men; F – women. The same applies to Tables 2 and 3.

Table 2. **Blood coagulation parameters in patients with CHD (M±SD)**

Parameter	Reference value	Patient group				p	
		Retrospective (n = 72)		Prospective (n = 78)			
		h (n = 29)	f (n=43)	m (n=19)	g (n=59)	p_1 (h)	p_2 (f)
Platelets, × 10^9	150–390	398.2 ± 19.9 95% CI (405.4, 391)	400 ± 19.8 95% CI (405.9, 400)	438.0 ± 19.2* 95% CI (446.6, 429.4) OR = 0.93	440 ± 19.3* 95% CI (444.9, 435.1) OR = 0.93	=0.15	=0.11
PI, %	90–105	103.5 ± 5.1 95% CI (105.4, 101.7)	104.4 ± 5.2 95% CI (105.9, 102.9)	134.6±6.2* 95% CI (137.4, 131.8) OR = 0.77	135.0 ± 6.7* 95% CI (137.4, 134) OR = 0.77	< 0.0001	< 0.0001
MRV	0.85–1.2	1.21 ± 0.62 95% CI (1.44, 0.98)	1.17 ± 0.59 95% CI (1.35, 0.99)	0.7 ± 0.03* 95% CI (37.09, 0.69) OR = 1.73	0.65 ± 0.03* 95% CI (0.657, 0.643) OR = 0.76	< 0.0003	< 0.0001
APTT, s	27.6–37.2	27.8 ± 1.4 95% CI (28.1, 27.1)	27.9 ± 1.5 95% CI (28.4, 27.5)	37.1 ± 2.2* 95% CI (38.1, 36.1) OR = 0.75	37.3 ± 2.3* 95% CI (37.9, 37.3) OR = 0.74	= 0.0004	= 0.0002
Fibrinogen, g/L	2–4	3.9 ± 0.2 95% CI (3.97, 3.83)	3.9 ± 0.2 95% CI (3.96, 3.84)	5.4 ± 0.26* 95% CI (5.56, 5.24) OR = 0.72	5.8 ± 0.29* 95% CI (5.87, 5.73) OR = 0.66	< 0.0001	< 0.0001
HR, s	10.4–12.6	12.7 ± 0.64 95% CI (12.93, 12.47)	12.8 ± 0.63 95% CI (12.99, 12.61)	4.23 ± 0.21* 95% CI (4.32, 4.14) OR = 1.23	4.27 ± 0.21* 95% CI (4.32, 4.22) OR = 3.0	<0.0001	< 0.0001
FLAC, min	170–220	198.8 ± 12.4 95% CI (203.2, 194.4)	193.3 ± 9.7 95% CI (196.2, 190.4)	165.5 ± 10.1* 95% CI (170, 162) OR = 1.2	159.0 ± 14.0* 95% CI (162.6, 155.4) OR = 1.2	=0.021	= 0.0002

higher than the corresponding values in the retrospective group–1.6 times higher in men and 1.1 times higher in women–while white blood cell and monocyte counts were 1.2 and 1.4 times higher, respectively. All other parameters (red blood cell count, hemoglobin levels, hematocrit, and lymphocyte count) in the prospective group were 1.4 and 1.38 times lower; 1.6 and 1.4; 1.6 and 1.5; and 2.8 and 3.1 times, respectively, in men and women, compared to the retrospective group.

The 95% CI values indicate a thorough and statistically sound approach to analyzing the data obtained from complete blood counts of patients with ACC.

Based on scientific logic and the calculations obtained, it was established that the levels of red blood cells, hemoglobin, hematocrit, and lymphocytes in the prospective group were lower than in the retrospective group, indicating resource depletion. The odds of an event occurring (a decrease in these parameters due to military operations) are higher (OR > 1) in the prospective group than in the retrospective group. Thus, the factor of wartime carries a risk of these changes developing.

The white blood cell count, monocyte count, and ESR in the prospective group were statistically significantly ($p < 0.001$) higher than in the retrospective group; however, the odds of an event occurring (an increase in these values) were lower (OR < 1) in the prospective group than in the retrospective group. In other words, wartime conditions carry a risk of these changes developing.

The status of the blood coagulation system in patients with ACC was studied (*Table 2*).

In the prospective group, PI values were 1.3 times higher in men and women, while INR values were 1.7 times lower in men and 1.8 times lower in women than in the retrospective group. The APTT in the prospective group was 1.34 times higher in both men and women than in the retrospective group. These values indicated hypercoagulation in patients with ACC during wartime.

Fibrinogen levels in patients with ACC in the prospective group were 1.4 times higher in men and 1.5 times higher in women than in the retrospective group.

The FLAK value in the prospective group was (165.5 ± 10.1) min in men and (159.0 ± 14.0) min in women and was significantly 1.2 times lower than in the retrospective group, indicating the presence of hypercoagulable processes. This is a key indicator in the diagnosis of conditions associated with the risk of thrombus formation or bleeding. A decrease in this value (hypofibrinolysis) indicates an increased risk of thromboembolic complications.

Analysis of blood coagulation parameters in patients with ACC, taking into account 95% confidence intervals, confirmed the statistical significance of the studies conducted.

Table 3. **Biochemical blood test results, laboratory values for inflammatory biomarkers, and levels of total vitamin D and magnesium in the blood of patients with CHD (M±SD)**

Parameter	Reference range	Patient group				p	
		Retrospective (n = 72)		Prospective (n = 78)			
		C (n = 29)	F (n=43)	M (n=19)	F (n=59)	r_1 (M)	p_2 (F)
Total protein, g/L	66.0 – 87.0	67.0 ± 3.7 95% CI (67.34, 64.7)	68.0 ± 3.6 95% CI (68.07, 65.93)	55.0 ± 3.1* 95% CI (56.4, 53.6) OR = 1.2	55.8 ± 3.2* 95% CI (56.6, 55.0) OR = 1.2	< 0.001	< 0.001
Serum glucose, mmol/L	3.88 – 6.38	5.4 ± 0.2 95% CI (5.47, 5.33)	5.7 ± 0.3 95% CI (5.79, 5.61)	6.1 ± 0.4* 95% CI (6.28, 5.92) OR = 0.88	6.4 ± 0.3* 95% CI (6.48, 6.32) OR = 0.91	< 0.001	< 0.001
Total bilirubin, µmol/L	5.0–21.0	19.6 ± 1.1 95% CI (20.0, 19.2)	20.1 ± 1.2 95% CI (20.46, 19.74)	20.6 ± 1.03 95% CI (21.1, 20.140) OR = 0.93	21.4 ± 1.1 95% CI (21.68, 21.12) OR = 0.91	0.002	<0.001
LDH, U/L	135.0 – 214.0	220.3 ± 4.8 95% CI (222, 218.6)	206.7 ± 3.9 95% CI (207.9, 205.54)	286.4 ± 5.6* 95% CI (288.9, 283.9) R-squared = 0.78	289.4 ± 5.6* 95% CI (290.8, 288) R-squared = 0.72	< 0.001	< 0.001
ALT, U/L	Up to 31.0	31.3 ± 1.2 95% CI (31.34, 31.26)	32.1 ± 1.3 95% CI (32.49, 31.71)	40.7 ± 1.7* 95% CI (41.46, 39.9) OR = 0.78	41.7 ± 1.7* 95% CI (42.1, 41.3) OR = 0.78	< 0.001	< 0.001
AST, U/L	Up to 31.0	30.9 ± 1.7 95% CI (31.52, 30.32)	31.6 ± 1.8 95% CI (32.13, 31.1)	43.2 ± 1.86* 95% CI (44.03, 42.37) OR = 0.71	44.2 ± 1.86* 95% CI (44.67, 43.7) OR = 0.72	< 0.001	< 0.001
LF, U/L	40.0 – 129.0	40.0 ± 3.6 95% CI (41.3, 38.7)	41.1 ± 3.7 95% CI (42.2, 40)	65.7 ± 4.2* 95% CI (67.6, 63.8) OR = 0.63	65.8 ± 4.2* 95% CI (66.9, 64.7) OR = 0.64	< 0.001	< 0.001
Total cholesterol, mmol/L	> 7.8 – high risk; < 5.2 – no risk	5.2 ± 0.26 95% CI (5.29, 5.1)	5.3 ± 0.26 95% CI (5.38, 5.22)	7.8 ± 0.31* 95% CI (7.94, 7.66) OR = 0.67	7.9 ± 0.32* 95% CI (7.92, 7.88) OR = 0.68	< 0.001	< 0.001
LDL-C, mmol/L	< 1.8 – high risk; < 2.6 – moderate risk; < 3.0 – low risk	2.6 ± 0.04 95% CI (2.61, 2.59)	2.82 ± 0.08 95% CI (2.84, 2.8)	1.95 ± 0.06* 95% CI (1.98, 1.92) OR = 1.34	2.1 ± 0.06* 95% CI (2.12, 2.08), OR = 1.34	< 0.001	< 0.001
Creatinine, µmol/L	44.0 – 80.0	80.8 ± 3.9 95% CI (82.2, 79.4)	81.7 ± 4.1 95% CI (83.9, 80.5)	88.9 ± 4.4* 95% CI (90.86, 86.94) OR = 0.9	89.9 ± 4.7* 95% CI (91.1, 88.7) OR = 0.95	< 0.001	< 0.001
Serum cortisol, nmol/L	Blood draw at 9:00 a.m.: 140–700	687.5 ± 19.3 95% CI (694.5, 680.5)	673 ± 26.2 95% CI (680.8, 665.2)	825 ± 27.1* 95% CI (837.1, 812.9) OR = 0.83	875 ± 35.3* 95% CI (884, 866) OR = 0.74	< 0.001	< 0.001
Cortisol in 24-hour urine, µg/24 h	50.0–190.0	185 ± 5.5 95% CI (187, 183)	192.6 ± 5.8 95% CI (194.3, 190.9)	222.0 ± 7.2* 95% CI (225.2, 218.8) OR = 0.84	231.1 ± 6.6* 95% CI (232.8, 229.4) OR = 0.82	< 0.001	< 0.001
D-dimer	<0.5 µg/mL (or <500 ng/mL) in FEO	254.2 ± 12.3 95% CI (258.7, 249.7)	262.4 ± 12.6 95% CI (266.1, 258.7)	355.9 ± 17.4* 95% CI (363.7, 348.1) OR = 0.71	365.9 ± 16.4* 95% CI (370.1, 361.7) OR = 0.71	< 0.001	< 0.001
CRP, mg/L	< 0.3 – 5	29.7 ± 1.5 95% CI (30.2, 29.16)	33.3 ± 1.7 95% CI (33.8, 32.8)	89 ± 4.5* 95% CI (91, 87) OR = 0.33	100 ± 5.0* 95% CI (101.3, 98.7) OR = 0.34	< 0.001	< 0.001
Ferritin, ng/mL	13.0 – 150.0	12.8 ± 0.7 95% CI (12.84, 12.76)	13.3 ± 0.7 95% CI (13.5, 13.1)	18 ± 0.5* 95% CI (18.2, 17.8) OR = 0.71	27 ± 0.5* 95% CI (27.13, 26.9) OR = 0.49	< 0.001	< 0.001
Procalcitonin, ng/mL	0.0 – 0.5	2.42 ± 0.12 95% CI (2.46, 2.38)	5.78 ± 0.29 95% CI (5.87, 5.69)	1.1 ± 0.06* 95% CI (1.13, 1.07) OR = 2.2	1.7 ± 0.09* 95% CI (1.72, 1.68) OR = 3.4	< 0.001	< 0.001
Magnesium, mmol/L	0.7 – 1.05	0.72 ± 0.04 95% CI (0.73, 0.71)	0.7 ± 0.04 95% CI (0.71, 0.69)	0.6 ± 0.03* 95% CI (0.61, 0.59) OR = 1.19	0.41 ± 0.02* 95% CI (0.415, 0.405) OR = 1.69	< 0.001	< 0.001
Vitamin D (total), ng/mL	6.23 – 49.9	9.3 ± 0.47 95% CI (9.47, 9.13)	8.2 ± 0.41 95% CI (8.32, 8.08)	7.2 ± 0.36* 95% CI (7.36, 7.04) OR = 1.29	6.3 ± 0.32* 95% CI (6.38, 6.22) OR = 1.3	< 0.001	< 0.001

Note. FEU – fibrin equivalent units.

According to the results obtained, it was found that platelet count, PI, APTT, and fibrinogen levels in the prospective group were higher, while the INR was lower–but only in women–than in the retrospective group, indicating hypercoagulation, while the odds of an event occurring were lower (OR < 1) in the prospective group than in the retrospective group. In other words, the wartime factor does not carry a risk of developing these changes, except for the INR in men (OR = 1.73).

The PC and FLAC values in the prospective group were statistically significantly ($p < 0.0001$) lower than in the retrospective group, indicating signs of hypercoagulation. The odds of an event occurring (a decrease in these values) were higher (OR > 1) in the prospective group than in the retrospective group. Thus, the risk of developing these changes is associated with the wartime factor.

A biochemical blood analysis was performed to determine laboratory levels of inflammatory biomarkers (D–dimer, CRP, ferritin, procalcitonin) and the levels of vitamin D (total) and magnesium in the blood of patients with ACC (*Table 3*).

Hypoproteinemia was observed in patients with ACC in the prospective group, where the total protein level was 1.2 times lower ($p < 0.001$) than in the retrospective group, in both men and women. Glucose and total bilirubin levels in the prospective group were 1.1 times higher than the corresponding values in the retrospective group in both men and women.

In the prospective group, liver function test results were higher in men and women than in the retrospective group: LDH activity was 1.3 and 1.4 times higher, ALT levels were 1.3 and 1.3 times higher, AST levels were 1.4 and 1.4 times higher, and LFT levels were 1.6 and 1.6 times higher, respectively ($p < 0.001$).

Total cholesterol levels in patients in the prospective group were 1.5 times higher, and creatinine levels were 1.1 times higher than the corresponding values in the retrospective group.

LDLP levels in men and women in the prospective group were 1.3 times lower than in the retrospective group. According to the recommendations of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS), target levels of LDLP cholesterol (LDLP–C) are determined individually based on the patient's cardiovascular risk category.

The target LDLP–C levels (ESC/EAS 2019/2025) are as follows. Very high risk: < 1.4 mmol/L (as well as a reduction of at least 50% from baseline). This applies to patients with a confirmed diagnosis of myocardial infarction, stroke, diabetes mellitus with target organ damage, chronic kidney disease, or a very high risk according to the SCORE (Systematic Coronary Risk Evaluation) scale: >10%. High risk: < 1.8 mmol/L. Moderate risk: < 2.6 mmol/L. Low risk: < 3.0 mmol/L.

The levels of cortisol (a stress hormone) were measured in blood serum and in 24–hour urine. The serum cortisol level in women with ACC in the prospective group was (875 ± 35.3) nmol/L and was 1.3 times higher than that in women in the retrospective group ($p < 0.001$). In men in the prospective group, the cortisol level was (825 ± 27.1) nmol/L and was 1.2 times higher ($p < 0.001$) than in men in the retrospective group.

Daily urinary excretion of free cortisol in the prospective group was (231.1 ± 6.6) μg/24 h for women, and in men, (222.0 ± 7.2) μg/24 h, and was 1.2 and 1.2 times higher, respectively, than in the retrospective group, with statistical significance ($p < 0.001$).

The D–dimer level in the prospective group was 1.4 times higher than that in the retrospective group, indicating that a blood clot was being broken down in the body, as well as the presence of infection and inflammation.

In the prospective group, CRP levels in both women and men were 3 times higher than in women and men in the retrospective group. CRP data formed the basis for diagnosing acute inflammatory processes, monitoring treatment (especially for infections), and assessing the risk of cardiovascular disease. A significant increase in CRP levels (>100 mg/L) is characteristic of bacterial infections.

In the prospective group, ferritin levels were higher than in the retrospective group: 1.4 times higher in men and 2.0 times higher in women ($p < 0.001$), confirming the presence of both an inflammatory process and anemia in the body.

Procalcitonin levels in patients with ACC in the prospective group were 2.2 times higher in men and 3.4 times higher in women compared to the corresponding values in the retrospective group ($p < 0.001$).

The study results showed a statistically significant ($p < 0.001$) decrease in serum magnesium levels in patients with ACC in the prospective group: 1.2–fold and 1.7–fold in men and women, respectively, compared with magnesium levels in the retrospective group.

It was demonstrated that in patients with ACC in the prospective group, total vitamin D levels were reduced and approached the lower limit of the normal range: (7.2 ± 0.36) ng/mL in men and (6.3 ± 0.32) ng/mL in women, and was 1.3 times lower than in the retrospective group.

Blood chemistry test results, laboratory values for biological markers of inflammation (D–dimer, CRP, ferritin, procalcitonin), and levels of total vitamin D and magnesium in the blood in patients with ACC fell within the 95% confidence interval and confirmed the statistical significance of the studies conducted.

According to the calculations, it was found that the levels of total protein, LDLP, magnesium, and vitamin D (total) in

Table 4. **Etiopathogenesis of CHD in the Context of Hostilities in Ukraine**

Risk factors				
Psychoemotional stress: chronic stress, anxiety; activation of the sympathetic-adrenal system; disruption of neuroendocrine regulation	Eating disorders: irregularity; lack of liquid and hot meals, fast food; excess fat, lack of fiber and vitamins	Dehydration: limited water intake, intense physical activity, fluid loss due to heat, equipment, or stress	Physical inactivity: (for military personnel and civilians): a sedentary lifestyle, prolonged stays in shelters	War-related factors
Abnormalities in bile composition and function				
Increased cholesterol content in bile	Decreased levels of bile acids	Decreased levels of phospholipids	Increased bile viscosity	Increased lithogenicity of bile
Formation of gallstones (cholelithiasis)				
Cholesterol crystallization	Formation of microliths	Growth and aggregation of calculi	Formation of calculi (gallstones)	
Disruption of gallbladder motility				
Dyskinesia (hypotonia and hypokinesia)	Bile stasis; increased intra-gallbladder pressure	Obstruction of the neck/gallbladder duct by a calculus		
Inflammation of the gallbladder wall				
Ischemia of the gallbladder wall (due to increased pressure and impaired microcirculation)	Damage to the epithelium, increased permeability	Bile infection (bacterial translocation: E. coli, Klebsiella, Enterococcus, etc.)	Inflammatory response (cytokines: interleukin-1, interleukin-6, tumor necrosis factor-α, leukocyte infiltration, edema)	CHC
Possible complications				
Gallbladder empyema	Gallbladder perforation	Pericholecystitis, abscess	Cholangitis	Pancreatitis	Sepsis
Aggravating factors during wartime				
Limited access to medical care (delayed presentation, evacuation difficulties)	Diagnostic limitations (lack of ultrasound, laboratory tests)	Shortage of medications and resources	Hypothermia, physical exhaustion	Concomitant injuries, blood loss, microcirculatory disorders	Increased risk of severe acute coronary syndrome and the development of its complications

the prospective group were lower than in the retrospective group, indicating resource depletion, with the exception of procalcitonin, which was higher. The odds of an event occurring (a decrease in the levels of the aforementioned markers and an increase in procalcitonin levels) were higher in the prospective group (OR > 1) than in the retrospective group. Thus, wartime conditions influence the risk of developing these changes.

Other markers in the prospective group were statistically significantly ($p < 0.001$) higher compared with the corresponding markers in the retrospective group. However, the odds of an event occurring (an increase in these indicators) were lower (OR < 1) in the prospective group than in the retrospective group. That is, the wartime factor does not pose a risk for the development of these changes.

In 1 patient in the prospective group, microthromboembolism of the small pulmonary arteries was observed; in 3 patients, pneumonia; and in 3, cardiac arrhythmia. None of them died. No deaths were recorded in the prospective group. In the retrospective group, the mortality rate was 1.6%.

Based on the conducted studies, a model of the etiopathogenesis of ACC under wartime conditions in Ukraine has been developed (*Table 4*).

The data *in Table 4* suggest that a combination of war–related stressors, lifestyle disruptions, dietary changes, limited access to medical care, and the influence of concomitant factors contributes to the development of cholelithiasis and ACC, increases the risk of complications, and worsens the prognosis.

Discussion

A quantitative and qualitative complete blood count characterizes the state of the hematopoietic system and the primary functions of the blood, and enables the detection of pathological processes in the human body. Monocyte levels are associated with the activity of pinocytosis and immune phagocytosis, as well as the presence of receptors for immunoglobulins and complement on the cell membrane [8].

The primary function of platelets is to participate in the blood coagulation process. Platelet counts increase during inflammatory processes of viral and bacterial origin, which are characteristic of ACC during wartime. The PT value characterizes the effect of external mechanisms and general factors on blood coagulation. The external coagulation pathway is assessed based on the PT, PI, and INR indices. The intrinsic coagulation pathway is evaluated using the aPTT [8, 9]. An increase in the concentration of fibrinogen–an acute–phase protein associated with inflammation–in blood plasma leads to an acceleration of the ESR. Clot lysis time indicates the presence of FLAK. The results of studies confirm the presence of blood hypercoagulation processes in patients with ACC, which developed during the war due to the adverse effects of endogenous and exogenous factors [9, 11].

Blood plasma contains more than 300 different proteins, including enzymes, enzyme inhibitors, blood clotting factors, transport proteins, and others. The synthesis of blood plasma proteins occurs primarily in liver cells and cells of the reticuloendothelial system. The concentration of total protein depends on the breakdown of two main protein fractions: albumin and globulins. Blood protein fractions influence blood clotting processes, steroid hormone levels, and other factors. Total blood bilirubin is one of the main components of bile and a product of the metabolism of hemoglobin, myoglobin, cytochromes, and heme–containing pigments. Cholesterol–a secondary monohydric cyclic alcohol–is a component of cell membranes, a precursor to steroid hormones and bile acids, and the most important indicator of lipid metabolism. High cholesterol levels can trigger pathological changes in blood vessel walls. The LDLP cholesterol fraction indicates the absence or presence of a risk of atherosclerosis. According to an analysis of the results obtained, patients with ACC who are receiving treatment during wartime have impaired liver and kidney function, as well as disturbances in protein and lipoprotein metabolism [14].

By measuring levels of inflammatory biomarkers (D–dimer, CRP, ferritin, procalcitonin), the presence of inflammatory processes was confirmed in the bodies of patients with ACC that developed during wartime. D–dimer is a marker of thrombus formation and fibrinolysis; it is the end product of the breakdown of insoluble fibrin–which forms the basis of a thrombus–under the action of plasmin, and acts as an activator of the blood coagulation system, reflecting the intensity of pathological processes involving fibrinolysis. The concentration of D–dimer is directly proportional to the activity of fibrinolysis and the amount of lysed fibrin. High levels of D–dimer are associated, in particular, with thrombosis, infections, and inflammation. C–reactive protein (CRP) is a marker of tissue damage resulting from inflammatory processes, necrosis, and trauma. The primary function of CRP is to activate immune responses and bind various microorganisms and breakdown products of pathologically altered tissues. CRP is a pro–inflammatory trigger, as it stimulates the production of interleukin–1, interleukin–6, and tumor necrosis factor–α. Elevated CRP levels represent a nonspecific response to inflammatory and infectious processes [9, 12].

Cortisol is the most important glucocorticosteroid; it is essential for maintaining many bodily functions. Cortisol is synthesized by the adrenal cortex and acts as a key glucocorticoid hormone in response to stress, infections, and trauma–a characteristic of acute cholecystitis.

As a "stress hormone," its levels rise in response to inflammation, regulating energy metabolism and the immune response [24].

The most important physiological effects of cortisol are as follows: an increase in blood glucose levels (due to the stimulation of gluconeogenesis), as well as anti–inflammatory and immunosuppressive effects. The synthesis and secretion of cortisol are regulated by the feedback loop of the hypothalamic–pituitary–adrenal axis. If cortisol levels are low, corticoliberin (corticotropin–releasing hormone) is released by the hypothalamus, which triggers the release of adrenocorticotropic hormone (ACTH) from the pituitary gland. ACTH stimulates the synthesis and secretion of cortisol in the adrenal glands. Cortisol itself acts via a negative feedback mechanism on the pituitary gland and the hypothalamus. Cortisol secretion increases during stress, and elevated cortisol levels are characteristic of depression. Thus, cortisol, as the "stress hormone," is the most important glucocorticosteroid, whose primary effects include increasing blood glucose levels, as well as anti–inflammatory and immunosuppressive actions. Hypercortisolism correlates with the development of depression, and in cases of chronic anxiety or depression, cortisol levels exceed the upper limit of the normal range by less than three times [8, 25].

Ferritin is the primary protein responsible for storing iron in the body; it is classified as an acute–phase protein, meaning its blood levels rise during inflammatory conditions. Ferritin levels rise in chronic inflammatory processes, acute and chronic liver inflammation, cancer, and other conditions [8, 26].

Procalcitonin is a polypeptide that serves as a marker of systemic inflammatory response, bacterial infection, and sepsis. Measuring procalcitonin levels in patients with ACC is used as a sensitive marker of purulent–septic complications and the severity of inflammation. Elevated procalcitonin levels above 0.5–2 ng/mL indicate a bacterial infection, while levels above 20.7 ng/mL indicate the development of severe complications (localized peritonitis). In the presence of infectious processes in the body, endotoxins are produced in large quantities, accompanied by increased levels of the pro–inflammatory cytokines interleukin–6 and tumor necrosis factor–α, as well as increased procalcitonin synthesis [8, 11–13, 25].

The links in the ACC pathogenic cycle include deficiencies in vitamin D and the trace element magnesium. Vitamin D helps stabilize macronutrient and micronutrient metabolism in the body, supports neurological responses and immunoregulatory functions, accelerates oxidative reactions, and increases the number of macrophages, among other effects [5–7]. Magnesium, an essential trace element and cofactor for 300 enzymes, plays a vital role in myocardial function, stabilizing platelet function, and supporting the nervous system (as a neuroprotective agent), among other processes. Magnesium deficiency exacerbates anxiety symptoms. These processes are crucial for the body. Magnesium regulates cell growth and protein synthesis. Magnesium interacts with calcium, potassium, and phosphorus in energy metabolism, carbohydrate metabolism, and the regulation of glycolysis, and it reduces lactate levels, among other effects. Magnesium is essential for the production of adenosine triphosphate (the primary source of energy) and for the relaxation of blood vessels in the cardiovascular system. This underscores the importance of measuring serum levels of vitamin D and magnesium in patients with ACC [4–7, 16].

Conclusions

1. Due to the hostilities in Ukraine, the etiopathogenic mechanisms and clinical and laboratory characteristics of the course of ACC are changing.

2. The course of ACC occurs against a background of impaired functions of the digestive, hepatopancreatobiliary, and urinary systems, as well as an impaired immune status, accompanied by an increase in the severity of inflammatory processes, disturbances in the blood coagulation system, and anemia.

3. Studying changes in laboratory parameters resulting from disruptions in the compensatory and adaptive mechanisms in patients with ACC during the period of full–scale war in Ukraine is essential for establishing a diagnosis and determining treatment strategies, which include both conservative and surgical methods.

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Authors' contributions

V. V. Mishchenko – defining the study design; A. V. Ponomarenko – data collection and processing; V. P. Mishchenko – data analysis, drafting the article.

Conflict of Interest

None.

Consent to Publication

All authors have reviewed the final draft of the manuscript and consented to its publication.

Human Rights Statement

The study was conducted in accordance with the ethical standards set forth in the 1964 Declaration of Helsinki and its subsequent amendments (2000), or comparable ethical standards and Good Clinical Practice (GCP). The study protocol was approved by the local ethics committee (Protocol No. 1 dated January 8, 2026). Voluntary informed consent was obtained from the patients enrolled in the prospective part of the study.

References

1. Gomes CA, Junior CS, Di Saverio S, Sartelli M, Kelly MD, Gomes CC, et al. Acute calculous cholecystitis: Review of current best practices. World J Gastrointest Surg. 2017 May 27;9(5):118-26. doi: 10.4240/wjgs.v9.i5.118. Erratum in: World J Gastrointest Surg. 2017 Oct 27;9(10):214. doi: 10.4240/wjgs.v9.i10.214. PMID: 28603584.
2. Hall BR, Armijo PR, Krause C, Burnett T, Oleynikov D. Emergent cholecystectomy is superior to percutaneous cholecystostomy tube placement in critically ill patients with emergent calculous cholecystitis. Am J Surg. 2018 Jul;216(1):116-9. doi: 10.1016/j.amjsurg.2017.11.002. PMID: 29128102.
3. Pisano M, Allievi N, Gurusamy K, Borzellino G, Cimbanassi S, Boerna D, et al. 2020 World Society of Emergency Surgery updated guidelines for the diagnosis and treatment of acute calculus cholecystitis. World J Emerg Surg. 2020 Nov 5;15(1):61. doi: 10.1186/s13017-020-00336-x. PMID: 33153472.
4. Babienko VV, Mokienko AV. Substantiation of the definition and correction of magnesium deficiency as an essential macronutrient and stress-limiting factor (review of the literature and results of our own research). Public Health Journal. 2023;(3): 23-32. Ukrainian. doi: org/10.32782/pub.health.2023.3.3.
5. Zmijewski MA. Vitamin D and Human Health. Int J Mol Sci. 2019 Jan;3;20(1):145. doi:10.3390/ijms 20010145.
6. Bie L. The Status and Research Progress on Vitamin D Deficiency and Atrial Fibrillation. Braz J Cardiovasc Surg. 2019 Dec 1;34(5):605-9. doi: 10.21470/1678-9741-2018-0322. PMID: 31719011.
7. Carlberg C. Vitamin D in the Context of Evolution. Nutrients. 2022 Jul 22;14(15):3018. doi: 10.3390/nu14153018. PMID: 35893872.
8. Nebyltsova OV, editor. Laboratory reference book Synevo. Kyiv: Doctor-Media; 2013. 644 p. Russian. ISBN: 9789662165255.
9. Gogia M, Kursov S, Markov O, Kudrevich O. Changes in coagulogram parameters in patients with polytrauma and different body mass index depending on the method of dosing enoxaparin sodium against the background of conventional and restrictive infusion therapy regimens. Bulletin of the V.N. Karazin Kharkiv National University. Series Medicine. 2025;33(2(53):235-45. Ukrainian. doi: 10.26565/2313-6693-2025-53-06
10. Pavlovych YuV, Kryzhevsky VV, Bilyayeva OO. Optimization of diagnosis and treatment of acute cholecystitis and modern measures for prevention of intraoperative and postoperative complications. Ukr Med J. 2022;1-2(147-148):97-100. Ukrainian. doi: 10.32471/umj.1680-3051.147.228624.
11. Cherkun O, Sheyko V, Sytnik D, Kryzhanovsky O. Prognostic value of biochemical markers in purulent-ceptic complications of acute severe pancreatitis. Actual Problems of Modern Medicine: Bulletin of Ukrainian Medical Stomatological Academy. 2019;19(2), 99-102. doi: 10.31718/2077-1096.19.2.99.
12. Rotar OV, Khomyak IV, Rotar VI, Khomyak AI, Railyanu CI. C-reactive protein and procalcitonin - laboratory markers of severity and complications of acute necrotizing pancreatitis. Klin Khir. 2020 March/April;87(3-4):14-7. Ukrainian. doi: 10.26779/2522-1396.2020.3-4.14.
13. Lapovets LE, Akimova VM, Tsymbala OP. Procalcitonin level in patients with acute calculous cholecystitis with septic complications. Bulletin of problems of biology and medicine. 2013;3(2):181-4. Ukrainian.
14. Matviychuk BO, Kavka MR, Matviychuk OB, Samchuk OO. The state of the blood coagulation system and the risk of thrombosis and embolism in acute calculous cholecystitis and its complications. Medical Science of Ukraine. 2023;(1):18-24. Ukrainian. doi: 10.32345/2664-4738.1.2023.03.
15. Stepas YM, Lapovets LE, Akimova VM. Assessment of some indicators of enzymatic activity of the liver in patients with acute cholecystitis. Bulletin of problems of biology and medicine. 2017;(1):188-90. Ukrainian.
16. Vlasenko OA, Rodionova IO, Vlasenko DA. Risk assessment of venous thromboembolism and D-dimer in clinical practice. Therapeutics, 2023;3(1):45-50. Ukrainian. doi: 10.31793/2709-7404.2022.3-1.45.
17. Yokoe M, Hata J, Takada T, Strasberg SM, Asbun HJ, Wakabayashi G, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci. 2018 Jan;25(1):41-54. doi: 10.1002/jhbp.515. PMID: 29032636.
18. Epps HV, Astudillo O, Martín YDP, Marsh J. The Sex and Gender Equity in Research (SAGER) guidelines: implementation and checklist development: a Korean translation. Ewha Med J. 2024 Jan;47(1):e11. Korean. doi: 10.12771/emj.2024.e11. PMID: 40703401.
19. Usenko OYu, Desyateryk VI. Mikhno SP. Okhotnik EO. Updated Tokyo Clinical Guidelines for the Treatment of Acute Cholangitis and Acute Cholecystitis 2018 (Tokyo Guidelines, 2018). Klin Khir. 2021;88(7-8):3-10. Ukrainian. doi: 10.26779/2522-1396.2021.7-8.03.
20. Sannan NS. Assessment of aggregate index of systemic inflammation and systemic inflammatory response index in dry age-related macular degeneration: a retrospective study. Frontiers in Medicine. 2023;10:1143045. doi: 10.3389/fmed.2023.1143045. PMID: 37181369.
21. Stepas YM, Lapovets LE, Akimova VM, Lavro ZYa. Peculiarities of changes in hemostasis system indicators and C-reactive protein levels in patients with acute cholecystitis. Medical and Clinical Chemistry. 2017;(1):76-80. Ukrainian. doi 10.11603/mcch.2410-681X.2017.v0.i1.7686.
22. Taizhanova D, Zubkov D, Komlichenko, E, Magalov I, Sorokina M, Amirbekova J, et al. Evaluation of coagulogram parameters for predicting early pregnancy loss. Reproductive Medicine (Central Asia), 2024;(3):82-91. Russian. doi: 10.37800/RM.3.2024.82-91.
23. Davydenko D, Galapchuk T, Motuzyuk O, Usova O. Coagulogram indicators in patients with post-covid syndrome. Notes in Current Biology.2024;7(1):80-5. Ukrainian. doi: 10.29038/NCBio.24.1-11.
24. Chiodini I. Clinical review: Diagnosis and treatment of subclinical hypercortisolism. J Clin Endocrinol Metab. 2011 May;96(5):1223-36. doi: 10.1210/jc.2010-2722. PMID: 21367932.
25. Buenrostro-Jáuregui MH, Muñóz-Sánchez S, Rojas-Hernández J, Alonso-Orozco AI, Vega-Flores G, Tapia-de-Jesús A, et al. A Comprehensive Overview of Stress, Resilience, and Neuroplasticity Mechanisms. Int J Mol Sci. 2025 Mar 26;26(7):3028. doi: 10.3390/ijms26073028. PMID: 40243691
26. Tamma PD, Heil EL, Justo JA, Mathers AJ, Satlin MJ, Bonomo RA. Infectious Diseases Society of America 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections. Clin Infect Dis, 2024 Aug 7:ciae403. doi: 10.1093/cid/ciae403. PMID: 39108079.

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