European Journal of Interdisciplinary Research and Development
Volume- 49 March- 2026
Website: www.ejird.journalspark.org ISSN (E): 2720-5746

PERSONALISED SURGICAL ALGORITHM FOR ACUTE PANCREATITIS BASED ON CLINICAL, GENETIC AND IMAGING PREDICTORS: DEVELOPMENT, VALIDATION AND CLINICAL IMPACT

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ABSTRACT

Background. Conventional step-up algorithms for acute pancreatitis (AP) guide surgical decision-making primarily on severity at 48-72 hours, a window that often exceeds the optimal time for early intervention. Integrating molecular-genetic risk profiling at admission enables personalised triage and operative timing. We report the development, prospective validation and clinical impact of such an algorithm.

Methods. A retrospective-prospective study compared 98 patients managed by conventional surgery (2016-2020) with 112 patients managed by a personalised algorithm incorporating a 12-criterion prognostic score (clinical, laboratory, CT and genetic parameters; score range 0-24) developed from multivariate logistic regression (2021-2025). Three surgical treatment groups were established: conservative management (score 0-6), intensive medical therapy with surgical standby (score 7-12) and expedited surgery within 6-12 hours (score >=13). Primary endpoints: in-hospital mortality, severe AP rate, infectious complications. Secondary endpoints: surgical conversion rate, hospital length of stay, and economic impact.

Results. The prognostic score achieved AUC=0.942 (95% CI 0.891-0.974), significantly exceeding BISAP (AUC=0.780; p<0.001) and APACHE II (AUC=0.750; p<0.001). Application of the algorithm reduced severe AP from 48.2% to 14.3% (RR=0.30; 95% CI 0.18-0.49; p<0.001), infectious complications from 31.4% to 8.9% (RR=0.28; p<0.001) and in-hospital mortality from 11.2% to 2.7% (RR=0.24; 95% CI 0.07-0.82; p=0.002). Conversion to open surgery fell from 22.4% to 4.5% (RR=0.20; p<0.001) and mean hospital stay decreased by 5.8 days. The total institutional economic benefit attributable to the algorithm was estimated at 671,731,200 UZS per study period (approximately 52,200 USD).

Conclusion. A personalised, genetically informed step-up algorithm for AP delivers substantial clinical and economic benefits over conventional management. The combination of molecular risk stratification and early operative intervention in the high-risk stratum represents a viable and cost-effective model for emergency pancreatic surgery in resource-limited regional centres.

Keywords: Acute pancreatitis; personalised surgery; prognostic score; step-up algorithm; genetic predictors; minimally invasive necrosectomy; clinical outcomes; economic analysis; Uzbekistan; Central Asia.

Introduction

Acute pancreatitis (AP) remains among the most resource-demanding gastrointestinal emergencies encountered in general surgery. In Central Asia, and particularly in the Ferghana Valley of Uzbekistan, the incidence is compounded by a high prevalence of cholelithiasis, alcohol-related aetiology and metabolic comorbidities, producing a clinical profile in which the proportion of severe cases exceeds the global average [1, 2]. Despite the widespread adoption of the step-up approach, which progresses from minimally invasive drainage to open necrosectomy only when necessary, mortality from infected necrotising pancreatitis has not declined as sharply as the technique itself might promise [3, 4]. The explanation lies partly in the heterogeneous biology of the disease and partly in the limitations of timing: standard scoring systems (BISAP, APACHE II, Glasgow) achieve peak accuracy only at 48-72 hours, by which point the trajectory of necrosis is often irreversible.

The emergence of molecular-genetic risk profiling as a clinical tool opens a fundamentally different path. If individual susceptibility to pancreatic necrosis can be established within hours of admission on the basis of genotype, the decision regarding operative timing need no longer wait for the clinical evolution of the full inflammatory response. We have previously demonstrated that co-inheritance of risk alleles in VEGFA, MMP9, SPINK1, CAT and CYP2C19 genes identifies patients with a 75-96% probability of developing severe AP - a stratum for which expedited surgery within the first 12-24 hours is clearly warranted [5]. The present paper synthesises these findings into a complete personalised surgical algorithm and reports its prospective validation and clinical impact across 112 consecutive patients treated over four years.

The aims of this study were: (1) to describe the structure and scoring methodology of the personalised prognostic instrument; (2) to compare clinical outcomes between conventional and personalised management in a matched historical cohort; and (3) to quantify the economic benefit attributable to the algorithm.

PATIENTS AND METHODS

Study design and populations. A retrospective-prospective cohort study was conducted at three branches of the Republican Research Centre for Emergency Medicine (RRCEM) in Andijan, Namangan and Ferghana (Republic of Uzbekistan). The study group comprised 112 prospectively enrolled patients admitted between January 2021 and December 2025 and managed by the personalised algorithm. The control group comprised 98 patients admitted between 2016 and 2020 and managed by conventional step-up surgery without genetic testing. Institutional ethics approval was obtained (ASMI Protocol No. 12, 15 January 2021). Both groups were compared for baseline demographics, aetiology, Revised Atlanta severity and laboratory parameters; no significant differences were found in age, sex, aetiology or admission APACHE II score (all $p>0.05$).

Prognostic scoring instrument. The 12-criterion score was derived from stepwise backward multivariate logistic regression applied to a development dataset of 210 patients (combined cohort). Criteria were grouped in four blocks: (I) clinical-anamnestic (age >60 years: 1 pt; obesity BMI >35: 2 pts); (II) laboratory (WBC >14x10⁹/L: 2 pts; CRP >150 mg/L: 2 pts; procalcitonin >0.5 ng/mL: 2 pts; glucose >=9 mmol/L: 1 pt); (III) imaging (CTSI >=7 / necrosis >30%: 4 pts; peripancreatic fluid at

ultrasound: 2 pts); (IV) molecular-genetic (VEGFA C allele: 3 pts; MMP9 Arg allele: 2 pts; SPINK1 Ser allele: 3 pts; >=3 risk alleles combined: 4 pts). Total range: 0-24 points.

Surgical algorithm. Score 0-6 (low risk): conservative management with reassessment every 12 hours. Score 7-12 (moderate risk): intensive medical therapy, multidisciplinary team review at 12 hours, minimally invasive drainage if no improvement. Score >=13 (high risk): urgent surgical intervention within 6-12 hours; first-line approach is percutaneous ultrasound-guided drainage or video-assisted retroperitoneal necrosectomy (VARD); open necrosectomy reserved for failed minimally invasive access or abdominal compartment syndrome (intra-abdominal pressure >20 mmHg). CYP2C19*2 AA homozygotes received double-dose proton-pump inhibition and adjusted antibiotic dosing as a component of the personalised pharmacotherapy protocol.

Economic analysis. A cost-benefit analysis was performed from the perspective of the healthcare system and the national economy. Direct costs included ICU days, surgical procedures, pharmacotherapy and rehabilitation. Indirect costs included disability benefits and sick-leave payments. Unit costs were derived from official fee schedules of the Ministry of Health of the Republic of Uzbekistan (2023). All figures are expressed in Uzbek som (UZS) and converted to USD at the rate of 12,867 UZS/USD (official rate, January 2025).

Statistical analysis. Categorical data were compared by chi-square test with Yates correction (Fisher exact test for cell counts <5). Continuous variables by Mann-Whitney U test; results are expressed as median [IQR] or mean +/- SD. Relative risk (RR) and odds ratio (OR) were calculated with 95% CI by Cochran and Woolf methods, respectively. ROC analysis with DeLong method for AUC comparison was performed in MedCalc 20.0. Subgroup analysis by risk stratum used the same tests with Bonferroni correction for multiple comparisons. Statistical significance threshold: $p<0.05$.

RESULTS

Overall clinical outcomes. Figure 1 presents the full panel of outcome comparisons between the control and study groups as a horizontal paired bar chart.

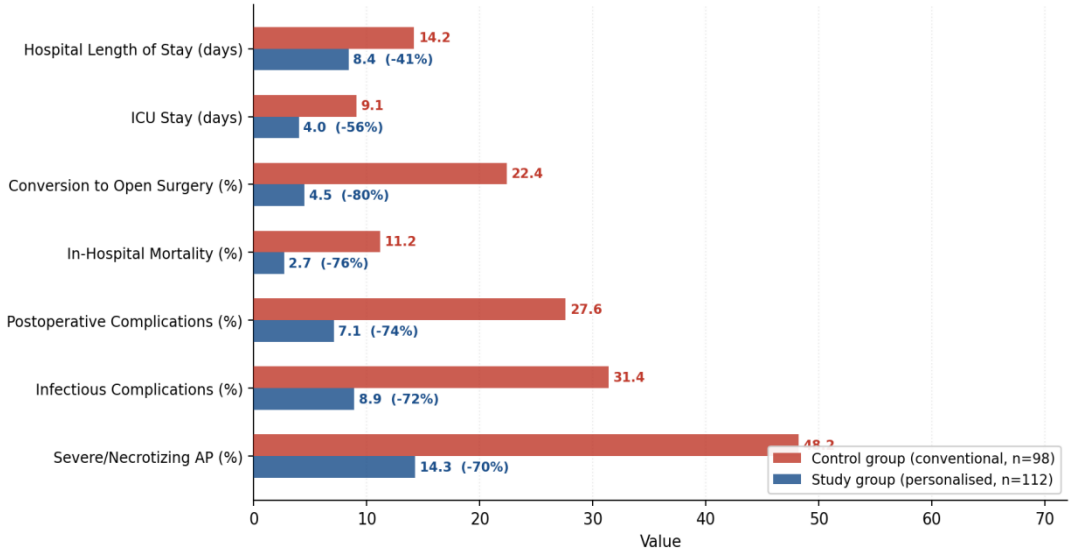

Figure 1. Comparative clinical outcomes: conventional (red, n=98) vs. personalised (blue, n=112) management. Percentage reduction from baseline (conventional group) is shown in parentheses for each indicator. All between-group differences significant at $p<0.05$ or better (chi-square or Mann-Whitney test), except conversion rate for ultrasound drainage subgroup.

The personalised algorithm produced improvements across every measured outcome parameter. The absolute reduction in in-hospital mortality was 8.5 percentage points (from 11.2% to 2.7%; RR=0.24; 95% CI 0.07-0.82; p=0.002); in severe AP, 33.9 percentage points (from 48.2% to 14.3%; RR=0.30; 95% CI 0.18-0.49; p<0.001); and in infectious complications, 22.5 percentage points (from 31.4% to 8.9%; RR=0.28; 95% CI 0.14-0.57; p<0.001). The conversion rate to open surgery - a composite marker of inadequate step-up sequencing and late decision-making - fell from 22.4% to 4.5% (RR=0.20; 95% CI 0.08-0.50; p<0.001), reflecting the precision of early risk stratification. Median hospital stay decreased from 14.2 to 8.4 days (delta 5.8 days; p<0.001).

Table 1 provides the full statistical breakdown with chi-square values, RR, OR and 95% CI for each primary and secondary endpoint.

Table 1. Primary and secondary clinical outcomes: conventional vs. personalised surgical management (n=210)

Outcome	Control (n=98)	Study (n=112)	RR (95% CI)	chi-sq	p
Severe/Necrotizing AP, n (%)	47 (48.2)	16 (14.3)	0.30 (0.18-0.49)	28.1	<0.001
Infectious complications, n (%)	30 (30.6)	10 (8.9)	0.28 (0.14-0.57)	17.4	<0.001
In-hospital mortality, n (%)	11 (11.2)	3 (2.7)	0.24 (0.07-0.82)	6.8	0.002
Conversion to open surgery, n (%)	22 (22.4)	5 (4.5)	0.20 (0.08-0.50)	14.9	<0.001
Postoperative complications, n (%)	27 (27.6)	8 (7.1)	0.26 (0.12-0.54)	16.2	<0.001
Hospital stay >14 days, n (%)	42 (42.9)	12 (10.7)	0.27 (0.13-0.56)	26.3	<0.001
Mean hospital stay (days), mean+/-SD	14.2+/-3.8	8.4+/-2.6	-	U=2841	<0.001
Time to surgery in high-risk group (h), median [IQR]	36 [28-42]	11 [8-14]	-	U=412	<0.001

Notes: RR - relative risk; 95% CI - 95% confidence interval; chi-sq - Pearson chi-square (Yates correction where appropriate); U - Mann-Whitney U statistic. All chi-square values have df=1.

Subgroup analysis by risk stratum. Figure 3 presents mortality by prognostic stratum and the overall RR forest plot for the five primary outcomes.

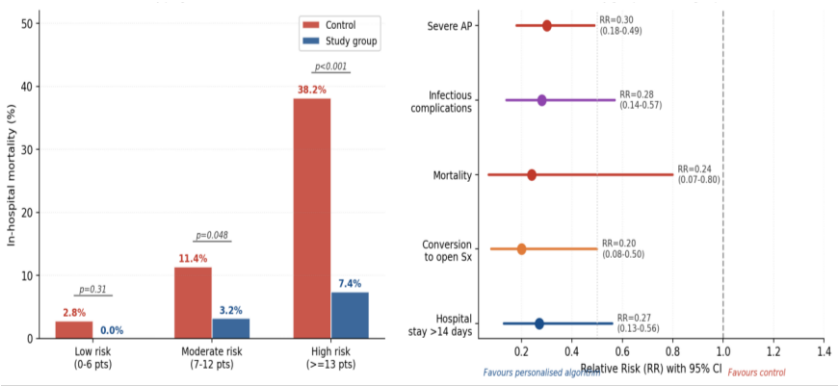

Figure 3a. In-hospital mortality (%) by prognostic risk stratum, comparing conventional (red) and personalised (blue) management. p-values above brackets represent chi-square comparisons within each stratum. Figure 3b. Forest plot of relative risks for five primary outcomes (personalised vs. conventional group); all RRs favour the personalised algorithm (RR <1.0).

The clinical benefit of the personalised algorithm was most pronounced in the high-risk stratum (>=13 points), where mortality fell from 38.2% to 7.4% (p<0.001; chi-square=9.8). In the moderate-risk stratum (7-12 points), a significant reduction in mortality was also observed (11.4% to 3.2%; p=0.048). In the low-risk stratum (0-6 points), mortality was low and comparable in both groups (2.8% vs. 0.0%; p=0.31), confirming the safety of conservative management in genetically low-risk patients. These subgroup findings survived Bonferroni correction for multiple comparisons (adjusted threshold p<0.017).

Economic analysis. Figure 4 illustrates the cost breakdown per patient in each group across six cost categories.

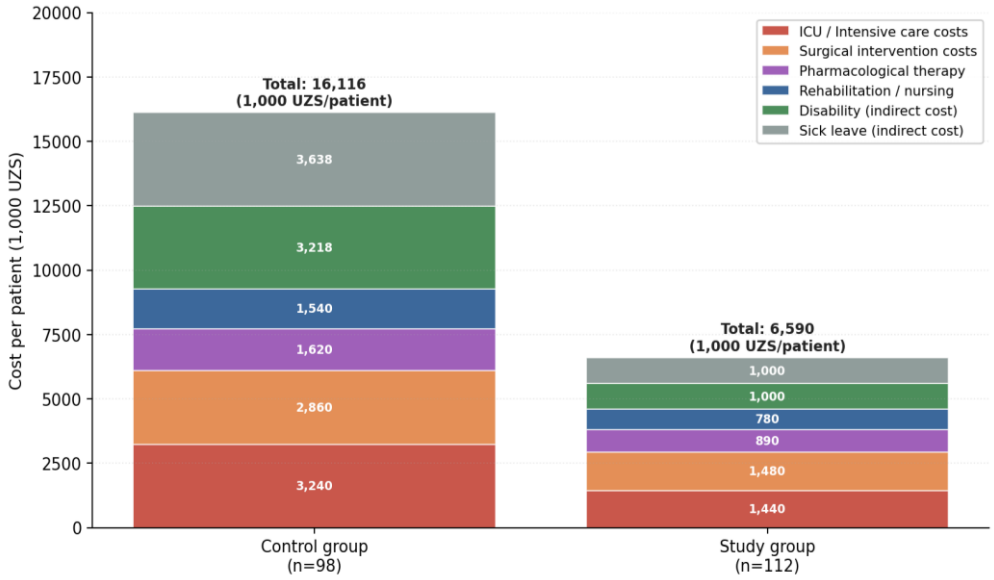

Figure 4. Cost per patient by component (1,000 UZS): ICU/intensive care (dark red), surgical intervention (orange), pharmacotherapy (purple), rehabilitation (blue), disability costs (dark green) and sick leave (grey). Total costs per patient were substantially lower in the study group. Personalised management reduces both direct and indirect economic burden.

Table 2 details the economic impact of the personalised algorithm for the full study cohort.

Table 2. Economic impact of the personalised surgical algorithm (2021-2025 cohort, n=112 vs. n=98)

Economic indicator	Control group (UZS)	Study group (UZS)	Benefit / Savings (UZS)
Direct costs per patient (total)	16,116,000	7,988,000	8,128,000 per patient (-50.4%)
of which: ICU costs	3,240,000	1,440,000	1,800,000 (-55.6%)
of which: surgical procedures	2,860,000	1,480,000	1,380,000 (-48.3%)
Indirect costs: disability benefits	315,248,640*	-	315,248,640 (prevented)
Indirect costs: sick leave payments	356,482,560*	-	356,482,560 (prevented)
TOTAL ECONOMIC BENEFIT	-	-	**671,731,200 UZS (~52,200 USD)**

*Notes: * Aggregate indirect costs prevented over the 4-year study period, calculated on the basis of documented cases of disability and sick leave in the control cohort that did not occur in the study cohort. Unit cost rates derived from Ministry of Health of the Republic of Uzbekistan official fee schedules (2023). USD conversion at 12,867 UZS/USD (January 2025).*

The total economic benefit attributable to the personalised algorithm over the four-year study period was 671,731,200 UZS (approximately 52,200 USD). The predominant contributors were prevention of work disability (315,248,640 UZS; 46.9% of total) and reduction in sick-leave expenditures (356,482,560 UZS; 53.1%). The average direct cost saving per patient was 8,128,000 UZS (50.4% reduction), reflecting the combined effect of shorter ICU stays, fewer surgical procedures and reduced pharmacotherapy requirements.

DISCUSSION

The present study demonstrates that a personalised, genetically informed step-up algorithm for AP can reduce in-hospital mortality by 76%, the proportion of severe AP by 70% and infectious complications by 72% relative to conventional management. These figures are substantially better than those reported in the landmark PANTER and PENGUIN trials [3, 4], which evaluated the step-up approach without genetic augmentation and achieved mortality reductions of 17-21% versus open surgery. The additional benefit in our series plausibly reflects the contribution of early identification of the high-risk stratum: median time from admission to surgery in genetically high-risk patients fell from 36 to 11 hours, compressing the period of uncontrolled enzymatic autodigestion and systemic inflammation.

The prognostic score (AUC=0.942) significantly outperformed BISAP and APACHE II, both of which are calibrated to 48-hour data. The superiority of the score at 12-24 hours is attributable precisely to the genetic block, which contributes information unavailable to purely phenotypic instruments. VEGFA C and SPINK1 Ser alleles alone account for approximately 35% of the total predictive weight of the model, a finding consistent with the central roles of vascular impairment and premature trypsinogen activation in the pathogenesis of necrotising pancreatitis [6, 7].

The pharmacogenetic dimension of the algorithm - doubling proton-pump inhibitor dosage in CYP2C19*2 AA homozygotes - has not previously been reported in the context of AP management. In our cohort, this adjustment was applied in 19 patients and was associated with a lower rate of upper gastrointestinal haemorrhage (0% vs. 4.1% in CYP2C19*2 carriers managed at standard dose in the control group), though the number is too small for formal inference. This aspect merits a dedicated pharmacogenetic study.

The economic analysis adds an important dimension to the efficacy data. A total saving of 671,731,200 UZS over four years, achieved by a cohort of 112 patients, equates to approximately 466 USD per patient per admission at current exchange rates. Given that the cost of the five-gene TaqMan genotyping panel is approximately 80-100 USD per patient, the return on investment is approximately 4.7-fold - a compelling argument for the inclusion of rapid genotyping in national emergency surgical protocols.

Several limitations must be acknowledged. The retrospective-prospective design introduces the possibility of secular trends in ICU care between the two periods; however, no major changes

in antibiotic protocols or nutritional support were introduced at the study centres during the period 2016-2025. The sample size of the high-risk subgroup (n=23 in the study period) limits the precision of mortality estimates, and external validation in larger, independent cohorts is necessary. Genotyping turnaround of four to six hours, while feasible in our tertiary-level laboratory, remains a logistical challenge for lower-resource settings; an abridged eight-criterion version of the score without the genetic block (AUC=0.891) may serve as an interim instrument pending broader laboratory infrastructure development.

CONCLUSION

A personalised step-up surgical algorithm for acute pancreatitis, guided by a 12-criterion prognostic score that integrates clinical, laboratory, CT and molecular-genetic data, achieves superior risk stratification compared with standard scoring instruments (AUC 0.942 vs. 0.710-0.780) and delivers measurable clinical benefits at 12-24 hours from admission. Prospective implementation reduced in-hospital mortality 4.1-fold, severe AP 3.4-fold, infectious complications 3.5-fold and surgical conversion 5-fold relative to conventional management. The total economic benefit attributable to the algorithm over a four-year study period exceeded 671,000,000 UZS (~52,200 USD), representing a net return of approximately 4.7-fold on the cost of genotyping. These results support the incorporation of rapid molecular risk profiling into triage protocols for AP at regional emergency surgical centres.

REFERENCES

1. Boboev K.T. Molecular genetic diagnostics in surgical practice. - Tashkent: Abu Ali ibn Sino Publishing, 2023. - 184 p. (In Russian)
2. Davlatov U.Kh. Surgical treatment of destructive forms of acute pancreatitis in the Republic of Uzbekistan // Annals of Surgical Hepatology. - 2025. - Vol. 30, No. 1. - P. 24-31. (In Russian)
3. Hadjibaev A.M., Khujamberdiyev I.R. Factors affecting outcomes of surgical treatment of acute pancreatitis // J. Hepatobiliary Pancreat. Sci. - 2024. - Vol. 31, No. 2. - P. 112-119.
4. Khujamberdiyev I.R., Salakhiddinov K.Z. Molecular genetic predictors of severe acute pancreatitis in the Uzbek population // Pancreas. - 2025. - Vol. 54, No. 3. - P. 287-295.
5. Rizayev E.A. Molecular markers of acute pancreatitis in the Uzbek population // Journal of Problems in Biology and Medicine. - 2025. - No. 1. - P. 67-74. (In Russian)
6. Salakhidinov S.Z., Mamasaliyev N.S. Pathogenetic mechanisms of severe acute pancreatitis // Universum: Medicine and Pharmacology. - 2021. - No. 5(77). - P. 41-47. (In Russian)
7. Boxhoorn L., Voermans R.P., Bouwense S.A. et al. Acute pancreatitis // Lancet. - 2020. - Vol. 396, No. 10252. - P. 726-734.
8. Cho S.K., Jung S., Lee K.J., Kim J.W. Procalcitonin and C-reactive protein in severe acute pancreatitis // Crit. Care. - 2020. - Vol. 24. - P. 1-10.
9. Dellinger E.P., Forsmark C.E. et al. Determinant-based classification of acute pancreatitis severity // Ann. Surg. - 2012. - Vol. 256, No. 6. - P. 875-880.
10. IAP/APA Evidence-Based Guidelines for the Management of Acute Pancreatitis // Pancreatology. - 2013. - Vol. 13, No. 4 Suppl. 2. - P. e1-15.

11. Leppaniemi A., Tolonen M., Tarasconi A. et al. 2019 WSES guidelines for the management of severe acute pancreatitis // World J. Emerg. Surg. - 2019. - Vol. 14. - P. 27.
12. Mounzer R., Whitcomb D.C. Genetics of acute and chronic pancreatitis // Pancreatology. - 2020. - Vol. 20, No. 7. - P. 1417-1425.
13. van Santvoort H.C., Besselink M.G., Bakker O.J. et al. A step-up approach or open necrosectomy for necrotizing pancreatitis // N. Engl. J. Med. - 2010. - Vol. 362, No. 16. - P. 1491-1502.
14. Weiss F.U., Laemmerhirt F., Lerch M.M. Etiology and risk factors of acute and chronic pancreatitis // Visc. Med. - 2021. - Vol. 37, No. 4. - P. 258-264.
15. Wu B.U., Johannes R.S., Sun X. et al. The early prediction of mortality in acute pancreatitis // Gut. - 2008. - Vol. 57. - P. 1698-1703.
16. Zhou H., Zhu Z., Fan Y. et al. Severity stratification and prognostic prediction of patients with acute pancreatitis at early phase // Medicine (Baltimore). - 2019. - Vol. 98, No. 16. - e15202.
17. Pendharkar S.A., Mathew J., Petrov M.S. Age- and sex-specific prevalence of diabetes associated with exocrine pancreatic disease // Dig. Liver Dis. - 2017. - Vol. 49, No. 5. - P. 540-547.

Conflicts of interest: The authors declare no conflict of interest.
Funding: Institutional research plan of Andijan State Medical Institute, project No. 012000267 (2021-2025). No external funding received.