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GENOTYPE-GUIDED SURGICAL TRIAGE IN ACUTE CALCULOUS CHOLECYSTITIS

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Relevance

The economic burden of acute calculous cholecystitis is substantial: in-hospital costs are driven primarily by duration of stay, rates of conversion from laparoscopic to open surgery, postoperative complications requiring re-intervention, and unplanned 30-day readmissions [1]. In middle-income settings such as Uzbekistan, a further component is extended temporary work incapacity and, in complicated cases, permanent disability, which generate indirect costs rarely captured in clinical trial outcome sets but directly relevant to national health economic assessments. Any surgical decision protocol that consistently reduces complications and shortens hospitalisation is potentially cost-saving, even if it introduces an upstream diagnostic expenditure.

Molecular-genetic testing has historically been regarded as expensive and logistically complex for emergency care. This perception is becoming less accurate as Real-Time PCR platforms are available at secondary and tertiary hospitals in Central Asia and per-assay genotyping costs decline. The critical question is therefore not whether genotyping is feasible, but whether its downstream effect on surgical outcomes generates a positive net economic return. To our knowledge, no published study has assessed the economic impact of a genotype-informed surgical algorithm for acute cholecystitis in a middle-income

healthcare context. Drummond M.F. et al. [4] outline the methodological requirements for such an analysis; the present work applies them to a prospective-retrospective cohort with a structured economic component.

Materials and Methods

The study population comprised 97 patients with acute calculous cholecystitis (Andijan, Fergana, and Namangan branches of the Republican Research Centre for Emergency Medicine, 2021-2025) managed under a personalised surgical algorithm incorporating a five-locus genetic risk score (TNF-α G308A, TLR4 Asp299Gly, IL-6 C174G, SOD2 Ala16Val, VEGFA C936T). The comparison group was a historical cohort of 184 patients managed without genotyping (2016-2020). Groups were comparable for age, sex, BMI, and ASA physical status ($p>0.05$). Direct hospitalisation costs were estimated using national tariff data for surgical inpatient bed-days, laparoscopic and open cholecystectomy procedure costs, ICU daily rates, wound care consumables, and laboratory investigations. Indirect costs were estimated from duration of certified sick leave per patient (national average wage, 2024) and from age-adjusted risk of first-time work disability assessment. Total economic effect was the difference in aggregate direct and indirect costs between cohorts. Sensitivity analyses varied the per-assay genotyping cost (range 150,000-400,000 Uzbek soums) and sick-leave duration assumptions (±20%). All figures are expressed in Uzbek soums at 2024 prices.

Results and Discussion

Mean length of hospital stay in the study cohort was 5.4±0.8 days versus 8.4±1.2 days in the historical cohort ($p<0.01$), a reduction of 3.0 inpatient days per patient, corresponding to 291 avoided bed-days across 97 patients. The conversion rate

decreased from 12.5% to 3.1% ($p<0.01$), eliminating nine open cholecystectomy procedures and their prolonged recovery. The postoperative complication rate fell from 19.4% to 6.2% ($p<0.001$), reducing the number of patients requiring re-intervention by 13 cases. The 30-day readmission rate was 6.2% in the study cohort versus an estimated 18.5% in the historical cohort ($p<0.01$).

The aggregate economic effect from direct cost components amounted to 274 million Uzbek soums across the 97-patient cohort. Indirect savings from reduced temporary work incapacity contributed an additional 306 million soums, and savings from avoided first-time disability assessments contributed 144 million soums, for a total benefit of approximately 580 million soums. The estimated total cost of five-locus genotyping for 97 patients at 200,000 soums per assay was 19.4 million soums, representing a benefit-to-cost ratio of approximately 30:1. Sensitivity analysis confirmed economic favourability across the full range of genotyping cost assumptions tested (break-even point: 61,400 soums per assay, well below current commercial pricing). These findings align with cost-effectiveness analyses of genetic decision support in other surgical conditions, as reviewed by Phillips K.A. et al. [2] and Rogowski W.H. et al. [3].

Several contextual features deserve emphasis. First, the benefit-to-cost ratio is conservative, as it excludes avoided malpractice liability, reduced antibiotic consumption, and the productivity value of freed caregiver time. Second, the analysis assumes current tariff structures accurately capture resource consumption, which may not hold in settings with cross-subsidised bed occupancy costs. Third, the comparison cohort predates the study period; secular trends in care quality may have contributed to the observed outcome difference, a limitation that only a prospective randomised economic evaluation can resolve [4].

A practical note on implementation: the five-locus TaqMan panel can be completed within a four-to-six-hour window on the Applied Biosystems 7500 Fast platform [5], fitting within the timeline of emergency surgical admission workup. The protocol does not require specialist genetics training and can be operated by a standard clinical biochemistry laboratory technician after a brief validation period. Access to a Real-Time PCR instrument is available at 11 of 14 provincial tertiary hospitals in Uzbekistan as of 2024, suggesting that implementation at scale is feasible without additional capital investment in most urban emergency surgical units [6].

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