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CLINICAL AND EPIDEMIOLOGICAL PREDICTORS OF MORTALITY AFTER LIVER TRANSPLANTATION

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Abstract. Liver transplantation is the most effective treatment for end-stage liver disease; however, postoperative survival is influenced by multiple donor- and recipient-related factors. In Central Asia, including Uzbekistan, the growing burden of chronic liver diseases such as viral hepatitis, non-alcoholic fatty liver disease, and metabolic syndrome, combined with limited transplant resources, makes outcome optimization a critical clinical and public health issue. A retrospective multicenter study was conducted involving 250 liver transplant recipients treated in major transplantation centers in Uzbekistan. Data on recipient characteristics (age, sex, BMI, MELD score, renal function, infectious complications), donor characteristics (age and BMI), and postoperative outcomes were analyzed. Statistical methods included chi-square tests, t-tests, ROC curve analysis, and multivariate logistic regression. Propensity score weighting was applied to reduce potential confounding bias. Statistical significance was set at $p < 0.05$. Among 250 patients, mortality varied significantly across follow-up periods ($p = 0.010$). Higher MELD scores, increased donor age, elevated recipient BMI, and renal impairment were significantly associated with increased risk of mortality ($p < 0.05$). Infectious complications showed a significant association in univariate analysis but were not consistently significant in multivariate models. ROC analysis demonstrated moderate predictive ability of MELD score and donor age for post-transplant mortality. Multivariate logistic regression identified MELD score, donor age, recipient BMI, and renal dysfunction as independent predictors of survival outcomes. Post-liver transplantation mortality in Uzbekistan is influenced by a combination of clinical and donor-related factors. MELD score, donor age, renal dysfunction, and recipient BMI represent key predictors of survival. Strengthening pre-transplant risk stratification and improving perioperative management may enhance transplantation outcomes in Central Asia.

Keywords: liver transplantation; Mortality risk factors; MELD score; Donor age; Renal dysfunction; Body mass index; Post-transplant outcomes; Epidemiology; Central Asia; Uzbekistan; Multivariate analysis; Survival analysis; Clinical predictors.

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Annotatsiya. Jigar transplantatsiyasi terminal bosqichdagi jigar kasalliklarini davolashning eng samarali usuli hisoblanadi, biroq operatsiyadan keyingi yashovchanlik donor va retsipiyent bilan bog‘liq ko‘plab omillarga bog‘liq. Markaziy Osiyoda, jumladan O‘zbekistonda, virusli gepatitlar, alkogolsiz yog‘li jigar kasalligi va metabolik sindrom kabi surunkali jigar kasalliklarining ortib borishi hamda transplantatsiya resurslarining cheklanganligi transplantatsiya natijalarini optimallashtirishni muhim klinik va jamoat salomatligi masalasiga aylantirmoqda. O‘zbekistondagi yirik transplantatsiya markazlarida davolangan 250 nafar jigar transplantatsiyasi qilingan bemor ishtirokida retrospektiv ko‘p markazli tadqiqot o‘tkazildi. Retsipiyentlarning xususiyatlari (yosh, jins, tana massasi indeksi — BMI, MELD skori, buyrak funksiyasi, infeksion asoratlar), donorlarning xususiyatlari (yosh va BMI) hamda operatsiyadan keyingi natijalar tahlil qilindi. Statistik usullar sifatida chi-kvadrat testi, t-test, ROC egri chizig‘i tahlili va ko‘p omilli logistik regressiya qo‘llanildi. Potensial chalkashtiruvchi omillar ta’sirini kamaytirish maqsadida propensity score weighting usuli qo‘llanildi. Statistik ahamiyatlilik darajasi $p < 0,05$ etib belgilandi. 250 nafar bemor orasida o‘lim ko‘rsatkichlari kuzatuv davrlari bo‘yicha sezilarli farq qilgani aniqlandi ($p = 0,010$). Yuqori MELD skorlari, donor yoshining kattaligi, retsipiyent BMI ko‘rsatkichining oshganligi va buyrak funksiyasi buzilishi o‘lim xavfining ortishi bilan sezilarli bog‘liq ekanligi aniqlandi ($p < 0,05$). Infeksion asoratlar bir omilli tahlilda sezilarli bog‘liqlik ko‘rsatgan bo‘lsa-da, ko‘p omilli modellar natijalarida doimiy ravishda ahamiyatli bo‘lmadi. ROC tahlili MELD skori va donor yoshi transplantatsiyadan keyingi o‘limni bashorat qilishda o‘rtacha darajadagi prognoz qobiliyatiga ega ekanligini ko‘rsatdi. Ko‘p omilli logistik regressiya natijalariga ko‘ra, MELD skori, donor yoshi, retsipiyent BMI va buyrak funksiyasi buzilishi yashovchanlik natijalarining mustaqil prediktorlari sifatida aniqlandi. O‘zbekistonda jigar transplantatsiyasidan keyingi o‘lim holatlari klinik va donor bilan bog‘liq omillar kombinatsiyasi ta’sirida yuzaga keladi. MELD skori, donor yoshi, buyrak funksiyasi buzilishi va retsipiyent BMI ko‘rsatkichlari yashovchanlikning asosiy prediktorlari hisoblanadi. Transplantatsiyadan oldingi xavfni stratifikatsiya qilish tizimini kuchaytirish hamda perioperatsion boshqaruvni yaxshilash Markaziy Osiyoda transplantatsiya natijalarini yaxshilashi mumkin.

Kalit so‘zlar: jigar transplantatsiyasi; O‘lim xavfi omillari; MELD skori; Donor yoshi; Buyrak funksiyasi buzilishi; Tana massasi indeksi; Transplantatsiyadan keyingi natijalar; Epidemiologiya; Markaziy Osiyo; O‘zbekiston; Ko‘p omilli tahlil; Yashovchanlik tahlili; Klinik prediktorlar.

Аннотация. Трансплантация печени является наиболее эффективным методом лечения терминальных стадий заболеваний печени, однако

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выживаемость после операции зависит от многих факторов, связанных как с донором, так и с реципиентом. Рост числа хронических заболеваний печени, таких как вирусные гепатиты, неалкогольная жировая болезнь печени и метаболический синдром, в Центральной Азии, включая Узбекистан, а также ограниченность ресурсов трансплантации делают оптимизацию результатов трансплантации важной клинической и общественной проблемой здравоохранения. Было проведено ретроспективное многоцентровое исследование с участием 250 пациентов с трансплантацией печени, получавших лечение в крупных трансплантационных центрах Узбекистана. Были проанализированы характеристики реципиентов (возраст, пол, индекс массы тела — ИМТ, оценка MELD, функция почек, инфекционные осложнения), характеристики доноров (возраст и ИМТ), а также послеоперационные результаты. В качестве статистических методов использовались критерий хи-квадрат, t-критерий, анализ кривой ROC и многомерная логистическая регрессия. Для уменьшения влияния потенциально мешающих факторов использовался метод взвешивания по склонности. Уровень статистической значимости был установлен на уровне $p < 0,05$. Было обнаружено, что показатели смертности среди 250 пациентов значительно различались в течение периодов наблюдения ($p = 0,010$). Было обнаружено, что высокие показатели MELD, пожилой возраст донора, повышенный ИМТ реципиента и нарушение функции почек были значительно связаны с повышенным риском смерти ($p < 0,05$). Хотя инфекционные осложнения показали значительную связь в однофакторном анализе, они не были постоянно значимыми в результатах многофакторных моделей. Анализ ROC показал, что оценка MELD и возраст донора обладают умеренной прогностической способностью в отношении прогнозирования смертности после трансплантации. Согласно результатам многофакторной логистической регрессии, оценка MELD, возраст донора, ИМТ реципиента и нарушение функции почек были определены как независимые предикторы результатов выживаемости. Смертность после трансплантации печени в Узбекистане обусловлена сочетанием клинических факторов и факторов, связанных с донором. Основными предикторами выживаемости являются оценка MELD, возраст донора, нарушение функции почек и ИМТ реципиента. Усиление системы стратификации предтрансплантационного риска и улучшение периоперационного ведения могут улучшить результаты трансплантации в Центральной Азии.

Ключевые слова: трансплантация печени; факторы риска смерти; оценка MELD; возраст донора; нарушение функции почек; индекс массы тела;

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результаты после трансплантации; эпидемиология; Центральная Азия; Узбекистан; многофакторный анализ; анализ жизнеспособности; клинические предикторы.

INTRODUCTION.

Chronic liver diseases remain a major public health concern worldwide and are associated with substantial morbidity, mortality, and healthcare expenditures. Liver transplantation is currently considered the most effective therapeutic option for patients with end-stage liver disease, acute liver failure, and selected hepatic malignancies. Over the past decades, advances in surgical techniques, immunosuppressive therapy, perioperative management, and donor-recipient matching have significantly improved post-transplant survival outcomes [1-4].

Despite these improvements, liver transplantation continues to be a highly complex and resource-intensive medical procedure, particularly in low- and middle-income countries where transplantation programs are still developing. In Central Asia, including Uzbekistan, the burden of chronic liver diseases has increased due to the growing prevalence of viral hepatitis B and C, non-alcoholic fatty liver disease (NAFLD), metabolic syndrome, obesity, and diabetes mellitus. At the same time, the availability of donor organs remains limited, creating major challenges in patient selection and allocation of liver grafts [5].

The imbalance between the increasing number of patients requiring transplantation and the shortage of suitable donor organs highlights the importance of identifying prognostic factors associated with post-transplant survival. Accurate risk stratification may improve patient selection, optimize perioperative management, and enhance long-term transplantation outcomes [6-9].

This study aimed to evaluate the influence of several clinical and demographic risk factors on mortality among liver transplant recipients in tertiary transplantation centers in Uzbekistan and the Central Asian region. Particular attention was given to the role of MELD score, donor age, renal dysfunction, infectious complications, and body mass index in predicting post-transplant survival.

METHODS.

The Model for End-Stage Liver Disease (MELD) score is widely used for prioritizing patients awaiting liver transplantation and estimating short-term mortality risk. The MELD system incorporates serum bilirubin, serum creatinine, and international normalized ratio (INR) values to objectively assess liver disease severity.

Several international studies have demonstrated that elevated MELD scores are associated with increased postoperative mortality and poorer graft survival.

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However, conflicting evidence exists regarding the predictive value of MELD in long-term survival after transplantation. In developing transplantation systems, including those in Central Asia, understanding the prognostic significance of MELD remains particularly important because patients are often referred at advanced disease stages.

Donor-related characteristics play an essential role in transplantation outcomes. Increasing donor age has been associated with reduced graft quality due to hepatic steatosis, fibrosis, vascular alterations, and decreased regenerative capacity.

Because of the persistent shortage of donor organs, transplantation centers are increasingly utilizing organs from older donors. Nevertheless, the optimal donor age threshold associated with acceptable survival outcomes remains uncertain, especially in emerging transplantation programs of Central Asia where donor pools are limited.

This study therefore examined the relationship between donor age and recipient survival in liver transplantation recipients from Uzbekistan.

Renal impairment is a frequent complication in patients with advanced liver disease and has been identified as an important predictor of postoperative complications and mortality following liver transplantation.

Chronic kidney dysfunction contributes to cardiovascular morbidity, metabolic disturbances, prolonged hospitalization, and reduced survival. In patients with cirrhosis, hepatorenal syndrome and impaired renal perfusion frequently worsen the clinical prognosis before transplantation.

Evaluating the impact of renal dysfunction on post-transplant survival is particularly relevant for Central Asian populations, where delayed referral and limited access to specialized hepatology care may contribute to advanced systemic complications prior to transplantation.

Infectious complications remain among the leading causes of morbidity and mortality after liver transplantation. Immunosuppressive therapy substantially increases susceptibility to bacterial, viral, and fungal infections.

Early postoperative infections commonly include surgical site infections, intra-abdominal abscesses, pneumonia, and bloodstream infections. Viral infections, particularly hepatitis B and hepatitis C recurrence, continue to represent important clinical concerns in liver transplant recipients.

In Central Asia, the epidemiological burden of chronic viral hepatitis remains considerable, making infectious complications an especially important determinant of transplantation outcomes in the region.

Body mass index (BMI) is another important factor potentially affecting liver transplantation outcomes. Obesity and metabolic syndrome are increasingly

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prevalent in Uzbekistan and neighboring Central Asian countries due to urbanization, dietary transitions, and reduced physical activity.

Elevated BMI has been associated with cardiovascular disease, diabetes mellitus, postoperative complications, and increased mortality risk in transplant recipients. Conversely, severe malnutrition and sarcopenia may also negatively affect postoperative recovery and long-term survival.

Therefore, assessment of BMI may contribute to improved perioperative risk stratification in liver transplantation candidates. A retrospective analytical study was conducted using data from liver transplant recipients treated in tertiary transplantation centers in Uzbekistan between 2010 and 2025.

The study included 250 adult patients who underwent primary liver transplantation. Clinical records, laboratory findings, donor characteristics, and postoperative outcomes were reviewed.

RESULTS AND DISCUSSION.

Among the 250 liver transplant recipients included in the study, 50 patients (20%) died within the first five years following transplantation, while 200 patients (80%) survived during the same follow-up period. A statistically significant variation in mortality rates across different post-transplant periods was observed (Cochran–Armitage trend test, $p = 0.010$), indicating that survival outcomes differed depending on the time interval after transplantation.

These findings suggest that post-transplant survival in the studied population is influenced not only by immediate perioperative factors but also by long-term clinical and organizational conditions affecting patient management in Uzbekistan's transplantation system.

Comparative analysis between survivors and non-survivors demonstrated significant differences in several key variables. Patients who died after transplantation had higher mean MELD scores compared to survivors, indicating more severe pre-transplant liver dysfunction. Similarly, elevated recipient BMI was associated with worse outcomes, suggesting that metabolic status plays an important role in post-transplant recovery.

Renal impairment was significantly more frequent among deceased patients, confirming its role as a strong predictor of poor prognosis. No statistically significant differences in mortality were observed between male and female recipients, indicating that sex was not a determining factor in survival outcomes in this cohort.

Donor characteristics showed a significant impact on transplantation outcomes. Increased donor age was strongly associated with higher recipient mortality, indicating reduced graft quality with aging donors. This finding is

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consistent with international evidence suggesting that older donor livers are more susceptible to steatosis, fibrosis, and reduced regenerative capacity.

Donor BMI demonstrated a weaker and less consistent association with mortality outcomes. Although slightly lower BMI values were observed among non-survivors, this relationship was not statistically robust in multivariate analysis, suggesting that donor BMI alone may not be a strong independent predictor of survival.

The MELD score demonstrated a strong and consistent association with post-transplant mortality. Patients with higher MELD values had significantly worse survival outcomes, confirming the predictive value of this scoring system in assessing disease severity before transplantation.

ROC curve analysis indicated moderate discriminatory power of the MELD score for predicting mortality, suggesting that although it remains a useful clinical tool, it should be combined with other risk indicators to improve prognostic accuracy in Central Asian transplant populations.

Renal impairment emerged as one of the strongest predictors of mortality in both univariate and multivariate analyses. Patients with reduced renal function prior to transplantation had significantly higher risk of death after surgery. This may be explained by the close interaction between hepatic and renal dysfunction in advanced liver disease, as well as increased susceptibility to postoperative complications, including cardiovascular instability and infection.

In the context of Uzbekistan, delayed referral to specialized care and limited access to early nephrological assessment may further exacerbate renal complications before transplantation.

Infectious complications, including bacterial and viral infections, were associated with increased mortality risk in univariate analysis. However, after adjustment for other covariates, infection did not remain a consistent independent predictor in multivariate models.

This may reflect the effectiveness of perioperative antimicrobial strategies or the confounding effect of baseline disease severity. Nevertheless, infection remains a clinically important factor in post-transplant management, particularly in regions with high endemic prevalence of viral hepatitis and limited infection control resources.

Multivariate logistic regression identified four independent predictors of post-transplant mortality: MELD score, donor age, recipient BMI, and renal dysfunction. These variables collectively represent key dimensions of transplant risk, including liver disease severity, donor organ quality, metabolic status, and systemic organ function.

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Propensity score–adjusted analysis confirmed the robustness of these associations, reducing potential bias related to patient selection and heterogeneity in clinical management across centers.

ROC analysis demonstrated that both MELD score and donor age had moderate predictive ability for post-transplant mortality. Optimal cut-off values provided acceptable sensitivity and specificity, suggesting their potential use in clinical decision-making.

However, predictive accuracy remained limited when these factors were considered individually, reinforcing the need for integrated multivariable risk assessment models in transplantation practice. The findings of this study are particularly relevant for Central Asia, where liver transplantation programs are still developing and healthcare resources remain constrained. The high prevalence of advanced liver disease at the time of transplantation reflects late diagnosis and limited access to specialized hepatology services.

In addition, donor shortages in Uzbekistan often necessitate the use of extended-criteria donors, including older individuals, which may negatively affect graft quality and outcomes. Similar challenges have been reported in other middle-income countries with emerging transplantation systems.

The significant impact of renal dysfunction and elevated MELD scores highlights the importance of early patient referral and multidisciplinary management of chronic liver disease. Furthermore, increasing rates of obesity and metabolic syndrome in Uzbekistan may contribute to worsening post-transplant outcomes, emphasizing the need for preventive public health strategies.

Overall, improving survival outcomes in liver transplantation requires not only surgical and clinical advancements but also systemic improvements in early diagnosis, donor selection policies, perioperative care, and long-term follow-up systems.

CONCLUSIONS.

This multicenter retrospective study provides evidence on the main clinical and epidemiological determinants of mortality after liver transplantation in Uzbekistan, representing a developing transplantation setting in Central Asia.

The study demonstrated that post-transplant survival is significantly influenced by a combination of recipient- and donor-related factors. Among the evaluated variables, the Model for End-Stage Liver Disease (MELD) score, donor age, recipient body mass index (BMI), and pre-existing renal dysfunction were identified as independent predictors of mortality.

Higher MELD scores were consistently associated with worse postoperative outcomes, confirming their value as a reliable indicator of disease severity. Increased donor age negatively affected graft outcomes, reflecting

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reduced organ quality in older donors. Renal dysfunction significantly increased the risk of post-transplant mortality, highlighting the importance of early detection and management of hepatorenal complications before transplantation. Elevated recipient BMI was also associated with poorer survival, emphasizing the growing impact of metabolic risk factors in the region.

In contrast, infectious complications showed significance mainly in univariate analysis, suggesting that their effect may be partially mediated through other clinical variables or perioperative management strategies. Overall, the findings highlight the importance of comprehensive pre-transplant risk assessment and the need for integrated clinical decision-making models in liver transplantation practice in Uzbekistan.

From a public health perspective, improving early diagnosis of chronic liver diseases, optimizing patient referral systems, strengthening donor selection criteria, and enhancing perioperative care may significantly improve transplantation outcomes in Central Asia.

Further large-scale prospective studies are recommended to validate these findings and to develop region-specific predictive models for liver transplant survival.

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