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# Analysis of the Causes of Complications and Mortality in Non-Critical Soft Tissue Diseases in Patients with Diabetes Mellitus

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**ABSTRACT**

*Non-critical soft tissue diseases in patients with diabetes mellitus, despite the relatively benign course in the general population, are often accompanied by unfavorable outcomes in this group of patients. A retrospective analysis of 56 cases of non-critical infectious and inflammatory diseases of soft tissues in patients with diabetes mellitus hospitalized in 2022–2024 was carried out. It was found that 11 out of 56 patients (19.6%) died, which emphasizes the need for a detailed study of the risk factors for a complicated course and death. The main causes of mortality were untimely medical attention, late diagnosis, high incidence of unrecognized concomitant diabetic nephropathy and uncontrolled hyperglycemia. Among the complications, phlegmons, abscesses, purulent lymphangitis, as well as deep vein thromboses against the background of inflammation prevailed. Statistically significant correlations were found between the level of HbA1c > 9.0%, renal dysfunction, localization of the process in the hip and pelvis, as well as the outcome of the disease. The data obtained indicate the need to revise the tactics of early routing of patients with this pathology and the introduction of an algorithm for multidisciplinary monitoring of patients with diabetes even with an outwardly mild course of soft tissue infections.*

***Key words:*** *diabetes mellitus, soft tissue infections, complications, mortality, diabetic nephropathy, hyperglycemia.*

## INTRODUCTION

Infectious and inflammatory diseases of soft tissues in patients with diabetes mellitus are traditionally considered as a clinically heterogeneous group of pathologies, which includes both severe forms, such as necrotizing fasciitis, and relatively favorable processes, such as superficial phlegmons, abscesses, infiltrates, purulent lymphangitis. However, even in the absence of signs of systemic destruction and fascia involvement, the outcome of such diseases in patients with impaired carbohydrate metabolism can be unpredictably severe [1, 2]. The progressive course against the background of hyperglycemia, immune dysfunction, diabetic angiopathy, and neuropathy forms a special clinical risk category: patients with "non-critical" but potentially lethal infections [3, 4].

According to a number of authors, the mortality rate among patients with non-critical forms of soft tissue in-

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fections in decompensated diabetes mellitus reaches 15–25% [5], while the key predictors of an unfavorable course are late admission, chronic renal failure, untimely surgery, and polymicrobial composition of pathogens [6]. At the same time, modern clinical classification and prediction of outcomes in such patients remains difficult due to the lack of generalized stratification scales and the low representation of such cases in large samples [7].

Most existing studies focus on critical forms (necrotizing fasciitis, gas gangrene), while noncritical forms of complicated soft tissue infections are considered secondary. Such an attitude can lead to an underestimation of the clinical danger and late treatment tactics [8].

The aim of the study was to analyze the causes of complications and deaths in patients with non-critical soft tissue diseases against the background of diabetes mellitus, highlighting key risk factors and features of treatment tactics.

## MATERIAL AND METHODS

The study is based on a retrospective analysis of 56 cases of hospitalization of patients with an established diagnosis of diabetes mellitus, who were diagnosed with non-critical forms of infectious and inflammatory diseases of soft tissues. The observation covered the period from 2022 to 2024 and was carried out on the basis of the surgical department of the multidisciplinary hospital. All patients included in the study suffered from type 1 or type 2 diabetes mellitus, while most of them had more than five years of experience. The presence of purulent-inflammatory changes in the skin and subcutaneous tissue, such as abscesses, phlegmons, purulent lymphangitis, infiltrates, without signs of necrotizing fasciitis or gas gangrene, was considered as an inclusion criterion. Patients with critical forms of soft tissue infections, as well as persons receiving systemic immunosuppressive therapy or having cancer, were excluded.

Upon admission, each patient underwent a standard clinical, laboratory and instrumental assessment. Demographic parameters, type and duration of diabetes, glucose and glycated hemoglobin (HbA1c) levels, the presence of chronic renal failure, including the stage and fact of renal replacement therapy, were analyzed. The presence of diabetic neuro- and angiopathy was taken into account. Particular attention was paid to the time from the onset of the disease to the moment of hospitalization, as well as the prevalence of the purulent process in anatomical zones. Bacteriological studies were performed with inoculation of the contents of the focus, if necessary, with the determination of antibiotic sensitivity.

The treatment tactics included both conservative measures (antibiotic therapy, glycemia correction, infusion therapy) and surgical interventions: opening and drainage of purulent foci, necrectomy, revision interventions in progression. Deceased patients (n=11; 19.6 %) formed a separate group for comparison, in order to retrospectively identify factors associated with death. The following criteria were considered as criteria for a complicated course: generalization of infection, deep vein thrombosis, repeated surgical interventions, secondary purulent processes and acute deterioration of metabolic or renal function.

Statistical processing was carried out using SPSS v.22 and Statistica v.12.5 packages. The mean (M), standard deviation (SD), median (Me) and interquartile range (IQR) parameters were used to describe the data. To assess the significance of the differences, the Mann–Whitney U-test for quantitative traits and the $\chi^2$ Pearson test for qualitative traits were used. The differences at $p < 0.05$ were considered statistically significant.

## RESULTS

Within the framework of this study, 56 cases of infectious and inflammatory diseases of soft tissues in patients with diabetes mellitus were analyzed. Of these, 11 cases (19.6%) were fatal due mainly to the development of a systemic inflammatory reaction and multi-organ dysfunction that meets the criteria for sepsis.

The deceased patients were characterized by a severe clinical condition at the time of admission: 9 of 11 patients showed signs of systemic inflammatory response syndrome (SIRS), including fever above 38.5 °C, tachycardia over 110 beats/min, and pronounced leukocytosis (greater than $18\times10^9$/L). In 8 cases, infusion-resistant hypotension was noted, which required the use of vasopressors. 6 patients developed acute respiratory distress syndrome, and 5 patients developed acute renal failure against the background of pre-existing diabetic nephropathy. According to clinical, laboratory and instrumental data, the diagnosis of sepsis was confirmed in 10 cases, including septic shock in 4 cases.

Long-term hyperglycemia turned out to be a key predictor of the development of sepsis and death: the average HbA1c level in the deceased was 10.1 ± 1.3%, and the glycemia at admission exceeded 18 mmol/l in 81.8% of patients. All deceased patients had signs of chronic renal failure, of which 7 were in the terminal stage, and 5 received programmatic hemodialysis. In 9 cases, the focus of inflammation was located in anatomically complex and poorly vascularized zones, such as the pelvis,

perineum, and proximal femur. In 6 patients, polymicrobial infections involving both gram-positive (MRSA) and anaerobic flora, including Bacteroides fragilis, were recorded.

The average duration of the disease until hospitalization in the group of victims was 6.8 days, while in the group of survivors it was 3.1 days. It was shown that late routing and delayed initiation of surgical debridement (more than 48 hours from manifestation) are significantly associated with a high risk of septic complications ($p = 0.004$). At the same time, all patients whose focus was drained on the first day of hospitalization completed treatment favorably.

Among the complications, in addition to sepsis, the deceased had deep vein thrombosis of the lower extremities ($n = 4$), disseminated intravascular coagulation syndrome ($n = 3$) and secondary purulent foci in other anatomical zones ($n = 2$). Only in one case was the outcome due to acute heart failure against the background of severe metabolic decompensation, without signs of systemic infection.

Thus, despite the absence of typical criteria for critical infections (such as necrotizing fasciitis), in the overwhelming majority of lethal cases, the key link in the pathogenesis was sepsis, which developed against the background of untimely diagnosed and inadequately controlled soft tissue infection.

In all 11 patients who completed the disease, complete pathological autopsies were performed, followed by histological examination of tissues. Autopsy results confirmed the presence of a septic process with signs of generalized purulent-resorptive fever. In all cases, foci of purulent inflammation were detected in the soft tissues of the affected area with a transition to fascia, vascular bundles and muscle fibers, accompanied by massive leukocyte infiltration, necrosis and foci of thrombosis of small vessels.

In 9 patients, systemic septic vasculitis was morphologically confirmed, including in the vessels of the kidneys, liver and adrenal glands. In 6 cases, signs of acute tubular necrosis and edema of the renal medulla against the background of chronic diabetic glomerulosclerosis were revealed, which was regarded as a morphological substrate of multiple organ failure. In 3 cases, acute respiratory distress syndrome with hyaline membranes in the alveoli and pronounced interstitial edema was diagnosed. In 4 patients, focal destruction of the myocardium was observed against the background of intramural thrombi of small vessels.

Thus, autopsies verified the clinically established diagnosis of sepsis, confirmed the connection of the lethal outcome with massive purulent intoxication, impaired microcirculation and decompensation of chronic renal failure. At the same time, the verified depth and aggressiveness of the local inflammatory process in most cases was underestimated in the early stages of follow-up.

Patient R., 67 years old, was admitted to the surgical department with complaints of severe pain, swelling and redness in the left thigh, fever up to 39 °C, and general weakness. From the anamnesis: type 2 diabetes mellitus for 18 years, chronic renal failure of the 5th stage (on hemodialysis 2 times a week), stroke a year ago, hypertension of the II stage.

On examination: hyperemia, tense fluctuating infiltration of the anterior-medial surface of the thigh up to 20×12 cm, the skin is glossy, regional lymph nodes are enlarged. Temperature 38.9 °C, heart rate 112 per minute, blood pressure 95/60 mm Hg. st., saturation 91%. HbA1c — 10.6 %, glucose — 21.3 mmol/l, creatinine — 712 μmol/l, urea — 38.6 mmol/l. Leukocytosis — $23\times10^9$/l, neutrophils 88 %, ESR — 54 mm/h.

The patient underwent emergency surgical debridement with wide opening and drainage of the cavities. In the postoperative period, there is pronounced hypotension, metabolic acidosis, oliguria. He was transferred to the ICU, where septic shock developed during the next day, despite combined antibiotic therapy (meropenem + vancomycin), hemosorption and vasopressor support. Death occurred on the third day from the moment of hospitalization.

Pathological report: femoral cellulitis with transition to deep fascia and muscle fibers, septic shock, multiple organ failure (acute tubular necrosis, interstitial myocarditis, septic alveolitis), stage V diabetic nephropathy, diabetic microangiopathy.

This clinical case demonstrates a typical scenario for the development of a complicated course in a seemingly localized form of infection. Untimely treatment, anatomically unfavorable affected area, diabetic angioneuropathy and end-stage renal disease predetermined the formation of a septic cascade already at the time of initial diagnosis. Even timely surgery and aggressive intensive care did not allow to interrupt the pathophysiological process. This example highlights the need to critically assess the initial risks and not underestimate the prognosis in the absence of signs of critical infection – sepsis can be the first and last manifestation of immune system vulnerability in a patient with severe diabetes.

## DISCUSSION

Patients with diabetes mellitus, especially with its prolonged and decompensated course, are a special risk group for the development of severe infectious complications. Disorders in the system of innate and adaptive immunity characteristic of diabetes include a decrease in neutrophil activity, macrophage dysfunction, delayed migration of immunocompetent cells, and inhibition of the synthesis of cytokines involved in the elimination of pathogens [1, 2]. Diabetic angiopathy exacerbates tissue hypoxia and reduces the ability of tissues to repair, which contributes to the transition of limited infection into a destructive and generalized form [3].

Against the background of immune vulnerability, sepsis is not so much a consequence of the severity of the anatomical lesion as the result of the body's systemic inability to mount an effective local immune response. In this sample, almost 20% of patients who died from seemingly limited infections had sepsis as the leading cause of death. These data echo the results of previous studies, which emphasize that localized purulent processes in diabetics can rapidly transition to the systemic phase without typical signs of progression at an early stage [4, 5].

Analysis of pathological materials showed that the true extent of inflammatory lesions of soft tissues and systemic vessels was often underestimated clinically, especially on the first day after admission. Morphological signs of systemic septic vasculitis, focal myocarditis, and tubular necrosis indicate the development of multiple organ failure of the "silent sepsis" type, when decompensation unfolds against the background of obliterated or nonspecific clinical manifestations [6]. This reinforces the need for in-depth monitoring of vital signs and a multidisciplinary approach to treatment, even in seemingly "non-critical" infections.

Of particular interest are the identified risk factors. High levels of HbA1c, late admission, localization of inflammation in the hip or pelvis, and terminal CKD are all significantly associated with death. Moreover, as the above clinical case has shown, sepsis and death can occur as early as the first 72 hours from the moment of admission, despite surgery and the use of antibiotic therapy according to all standards. This suggests that the outcome in such situations is largely predetermined by the systemic background of the patient, and not only by the severity of the local lesion.

Thus, at the clinical level, it is necessary to critically rethink the traditional gradation of soft tissue infections in diabetic patients into "mild" and "severe". Even in the absence of evidence of necrotizing fasciitis or extensive destruction, any purulent lesion in combination with decompensated diabetes and concomitant CKD should be considered potentially septic hazardous. In this regard, it is necessary to route such patients early to hospitals with the possibility of intensive care, to abandon expectant management in case of signs of increasing intoxication, and, possibly, to develop scales for stratification of the risk of sepsis in patients with diabetes and soft tissue infections.

## CONCLUSION

The study showed that even with formally "non-critical" forms of infectious and inflammatory diseases of soft tissues in patients with diabetes mellitus, the rapid development of sepsis and death is possible. The mortality rate was 19.6%, and in all cases the septic process with signs of multiple organ failure was morphologically confirmed. This emphasizes the inadmissibility of underestimating the severity of such conditions against the background of diabetic angiopathy and nephropathy.

The key factors associated with the development of sepsis and death were: HbA1c levels above 9.5%, the presence of end-stage CKD (including with dialysis), anatomically unfavorable localization of inflammation (hip, pelvis, perineum), and delayed admission to hospital. Taken together, these factors determined the extremely low potential for resistance to infection, regardless of the therapy used. Even with timely surgical intervention, the course of the disease in such patients is aggressive, rapidly generalizing.

The data obtained require a revision of clinical and diagnostic approaches to patients with diabetes and localized soft tissue infections. It is necessary to introduce early septic risk stratification scales, expand the indications for intensive monitoring and interdisciplinary management of patients with a high immunoinflammatory background. Any purulent inflammation in a decompensated diabetic should be considered not as a local process, but as a potential entry point into the septic cascade, which requires systemic vigilance and proactive tactics.

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**Ethics Statement:** The study was carried out in accordance with the principles of the Declaration of Helsinki. The protocol was approved by the local ethics committee. The deceased patients were autopsied in compliance with all legal and ethical standards.

**Conflict of interest:** The authors declare no conflict of interest.

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## QANDLI DIABET FONIDA YUMSHOQ TO‘QIMALARNING NEKRITIK KASALLIKLARI BILAN KASALLANGAN BEMORLARDA ASORATLAR VA O‘LIM SABABLARINI TAHLIL QILISH

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**ANNOTATSIYA**

Qandli diabet bilan og‘rigan bemorlarda yuzaga keladigan yumshoq to‘qimalarning infeksion-yallig‘lanish kasalliklari, ularning anatomik jihatdan chegaralangan va nekritik shaklda bo‘lishiga qaramay, tezda og‘ir sepsis holatiga olib kelishi mumkin. Ushbu retrospektiv tadqiqot 56 bemorni qamrab oldi, ularning 11 nafari (19,6 %) o‘lim bilan yakunlangan. O‘lim holatlarida asosiy sabab sepsis va u bilan bog‘liq bo‘lgan ko‘p organ yetishmovchiligi bo‘lgan. Klinik kuzatuvlar va patologoanatomik tahlillar bemorlarda diabetik angiopatiya, yuqori darajadagi glikemik nazorat yetishmasligi (HbA1c > 9,5 %) hamda surunkali buyrak yetishmovchiligi mavjudligi letallikning asosiy omillari ekanligini ko‘rsatdi. Ko‘pchilik hollarda sepsis belgilarining kech aniqlanishi va kech boshlangan jarrohlik davolash asoratlarning kuchayishiga sabab bo‘lgan. Tadqiqot natijalari, yumshoq to‘qima infeksiyalari bo‘yicha qandli diabetli bemorlar uchun erta diagnostika va intensiv ko‘p tarmoqli yondashuv zarurligini tasdiqlaydi.

**Kalit so‘zlar:** qandli diabet, yumshoq to‘qimalar infeksiyasi, sepsis, o‘lim, diabetik nefropatiya, HbA1c

## АНАЛИЗ ПРИЧИН ОСЛОЖНЕНИЙ И ЛЕТАЛЬНОСТИ ПРИ НЕКРИТИЧЕСКИХ ЗАБОЛЕВАНИЯХ МЯГКИХ ТКАНЕЙ У БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ

**ЕРКУЛОВ А.Ш.**

**ТАШКЕНТСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ**

**АННОТАЦИЯ**

Инфекционно-воспалительные заболевания мягких тканей у пациентов с сахарным диабетом, несмотря на свою ограниченную анатомическую локализацию и отсутствие признаков критического течения, нередко становятся причиной развития тяжёлого сепсиса и полиорганной недостаточности. Настоящее ретроспективное исследование охватывает 56 пациентов, 11 из которых (19,6 %) скончались. Основной причиной летального исхода во всех случаях явился сепсис, подтверждённый клинически и морфологически. Проведённый клинико-анатомический анализ показал, что определяющими факторами риска летальности были высокая степень декомпенсации углеводного обмена (HbA1c > 9,5 %), наличие терминальной стадии хронической почечной недостаточности, неблагоприятная локализация воспалительного очага (бедро, таз), а также позднее поступление в стационар. Во многих случаях недостаточная настороженность в отношении сепсиса и отсрочка хирургической санации способствовали прогрессированию процесса. Полученные данные подчёркивают необходимость пересмотра подходов к диагностике и ведению таких пациентов и внедрения мультидисциплинарной модели интенсивного наблюдения даже при отсутствии признаков критической инфекции.

**Ключевые слова:** сахарный диабет, инфекции мягких тканей, сепсис, летальность, диабетическая нефропатия, HbA1c