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Application of European guidelines for inguinal hernia in a tertiary hospital setting: Time for a change?

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Ethics Committee Approval
The study was approved by the Medical Ethics Committee of Ghent University Hospital (October 2020, EC/UZG/2019/239).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: The European Hernia Society (EHS) published practice guidelines in 2018, aiming to standardize inguinal hernia repair. These are not obligatory, and deviations in clinical practice may occur. This study investigates whether these guidelines were followed in a tertiary center and explores reasons for deviations.

Methods: A retrospective cohort study was conducted on 1607 patients who underwent inguinal hernia repair at Ghent University Hospital (2007–2020). Outcomes such as complications, recurrence, and chronic pain were analyzed in relation to EHS guideline adherence.

Results: TAPP was significantly associated with wound complications (OR 3.96, 95% CI 1.75–8.94; P=0.001). Lichtenstein repair showed the lowest recurrence rate (5.7%) but was often used in lower-risk patients, suggesting possible selection bias. Overall adherence to EHS guidelines was 60%. No significant difference in chronic postoperative pain was observed between open and laparoscopic techniques (P=0.21). Predictors such as age <50 years (OR 2.28), symptomatic hernias (OR 2.15), and laparoscopic repair (OR 1.39) were associated with wound complications.

Conclusion: EHS guidelines provide valuable direction but are not always reflected in practice. Clinical realities such as surgeon experience, patient factors, and hospital logistics influence deviation. These findings emphasize the need for more flexible, context-sensitive guidelines, supported by further prospective studies.

Keywords: inguinal hernia, European Hernia Society, guideline adherence, retrospective study, hernia recurrence, wound complications

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Introduction

Inguinal hernia repair is among the most frequently performed surgical procedures worldwide, with over 20 million cases reported annually [1]. Despite the ubiquity of this intervention, substantial variation persists in the choice of surgical technique, both across and within institutions.

To address this variability and improve patient outcomes, the European Hernia Society (EHS) published evidence-based clinical guidelines in 2018 [2]. These guidelines offer tailored recommendations based on patient-specific factors, hernia characteristics, and recurrence status. For instance, laparoscopic repair is recommended for bilateral and recurrent hernias when performed by experienced surgeons, whereas the open Lichtenstein technique remains appropriate for many primary unilateral hernias [2,3].

The EHS guidelines also emphasize shared decision-making and suggest strategies to minimize complications such as chronic postoperative pain and hernia recurrence. However, guideline adherence in clinical practice is not guaranteed. Surgical decisions are often influenced by surgeon preference, institutional resources, and individual patient factors. Several studies have reported frequent deviations from the guidelines, even in high-volume centers [4,5].

At Ghent University Hospital, various surgical techniques are used depending on the clinical context and the surgeon's expertise. Although the EHS guidelines are accessible, their integration into routine practice has not been systematically assessed.

This retrospective study aims to evaluate the extent to which the 2018 EHS guidelines are followed in a tertiary care center. Additionally, we investigate whether adherence to these guidelines is associated with clinical outcomes, including recurrence rates, wound complications, and chronic postoperative pain. By identifying deviations and their potential consequences, this study seeks to inform future updates of the guidelines and enhance their applicability in everyday clinical practice.

Materials and methods

Study design and setting

This retrospective observational cohort study was conducted at the Department of General Surgery of Ghent University Hospital, a tertiary referral center in Belgium. The study adhered to the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Ghent University Hospital Medical Ethics Committee on September 24, 2020 (approval number: BC-08479).

Patient selection

All adult patients (≥18 years) who underwent inguinal hernia repair (either primary or recurrent) at Ghent University Hospital between January 2007 and December 2020 were eligible for inclusion. Patients were identified through the hospital's electronic health records. Exclusion criteria were:

1. Incomplete surgical or follow-up data;
2. Concomitant major abdominal surgery performed during hernia repair.
3. Pediatric patients (<18 years).

Data collection

Relevant data were manually extracted from operative reports, anesthesia records, discharge summaries, and outpatient follow-up documentation. The following variables were collected:

- **Demographics**: age, sex
- **Hernia characteristics**: type (direct, indirect, combined, bilateral), side (left, right, bilateral), recurrence status, and symptomatology
- **Surgical technique**: Lichtenstein (open), TEP (totally extraperitoneal), or TAPP (transabdominal preperitoneal)
- **Surgeon experience**: staff surgeon versus trainee (if available)
- **Outcomes**: complications (e.g., wound infection, seroma), recurrence, and chronic postoperative pain (defined as pain persisting for more than three months postoperatively)

Definition of Guideline Adherence

Surgical procedures were categorized as either **guideline-conforming** or **non-conforming** based on the 2018 HerniaSurge/EHS guidelines [2]. For example, laparoscopic repair (TEP or TAPP) was considered guideline-conforming for bilateral or recurrent hernias, while the Lichtenstein technique was appropriate for primary unilateral hernias in older patients with comorbidities.

Statistical analysis

Data were analyzed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as means (standard deviations [SD]) or medians with interquartile ranges (IQR), depending on distribution. Categorical variables were summarized as frequencies and percentages. Group comparisons for categorical variables were conducted using the chi-square test or Fisher's exact test, as appropriate. Logistic regression analysis was performed to identify predictors of recurrence and complications, with results expressed as odds ratios (ORs) and 95% confidence intervals (CIs). A *P*-value <0.05 was considered statistically significant.

Results

Patient characteristics

A total of 1,607 patients were included in the study. The mean age was 59.5 (14.8) years, and the majority were male (93.1%). Most hernias were primary and unilateral.

Surgical techniques used

The three main surgical approaches employed were Lichtenstein, TAPP, and TEP. The choice of technique varied depending on patient characteristics and surgeon preference. Full distributions are presented in Table 1.

Table 1: Surgical outcomes by operative technique.

Technique	n	Recurrence (%)	Wound complications (%)	Chronic pain (%)
Lichtenstein	733	5.7	2.1	10.9
TAPP	529	6.8	7.8	11.6
TEP	**335**	**6.4**	**3.3**	**11.4**

TAPP: Transabdominal preperitoneal hernia repair, TEP: Totally extraperitoneal hernia repair

Complications

The overall complication rate was 7.1%. TAPP was significantly associated with a higher rate of wound-related complications compared to the other techniques (*P*=0.001). No

perioperative mortality was observed. The most frequent complications were seroma and hematoma formation.

Recurrence

The overall recurrence rate across all techniques was 6.3%. Although the Lichtenstein technique showed the lowest recurrence rate, the difference between techniques was not statistically significant (P=0.08). This observation may be influenced by patient selection bias.

Chronic Postoperative Pain

Chronic postoperative pain (defined as pain persisting for more than three months) was reported in 11.2% of patients. No statistically significant differences in chronic pain were found between surgical techniques (P=0.21), nor were any associations identified with age, sex, or hernia type.

Guideline Adherence

Overall, 60% of procedures were performed under the 2018 EHS guidelines. Common deviations included the use of open repair for bilateral hernias and laparoscopic repair in young patients with unilateral hernias. Non-conforming procedures were not significantly associated with differences in recurrence or chronic pain rates; however, a slight increase in wound-related complications was observed.

Predictive Analysis

Multivariate logistic regression identified the TAPP technique as an independent predictor of increased wound-related complications (OR 3.96, 95% CI 1.75–8.94; P=0.001). A body mass index (BMI) greater than 30 was also significantly associated with higher complication rates (OR 2.13, 95% CI 1.09–4.17; P=0.030). No independent predictors of recurrence or chronic postoperative pain were identified.

Discussion

This retrospective study evaluated adherence to the 2018 European Hernia Society (EHS) guidelines for inguinal hernia repair at a tertiary referral center and assessed whether deviations from these guidelines were associated with differences in clinical outcomes.

Approximately 60% of procedures were performed under the EHS recommendations, which aligns with findings from other European centers [2,6]. The most frequent deviations included the use of open repair for bilateral hernias and the performance of laparoscopic repair in younger patients with unilateral hernias. These choices appeared to be influenced by surgeon experience, patient comorbidities, and institutional logistics [3,5].

Despite these deviations, recurrence rates and the incidence of chronic postoperative pain were not significantly different from guideline-compliant cases. This suggests that in real-world practice, individualized decision-making may yield outcomes comparable to those recommended by standardized protocols [1,4]. However, the TAPP technique was independently associated with a higher incidence of wound-related complications. This finding is consistent with existing literature and may be related to peritoneal entry, increased operative time, or port-site morbidity [3].

The Lichtenstein technique remained widely used, particularly among older, low-risk patients. Its favorable outcomes in our cohort may reflect a degree of selection bias [4]. Other confounding factors, such as follow-up duration, variability in pain assessment tools, and surgeon proficiency, may also contribute to the observed differences [7]. Notably, we did not observe a significant reduction in chronic pain with laparoscopic approaches, contrasting with the findings of some earlier studies [8,9].

These findings highlight the challenges of implementing clinical guidelines in daily practice. While evidence-based recommendations are crucial, real-world decision-making is shaped by a complex interplay of patient- and system-level variables. Our results advocate for a flexible, context-sensitive application of surgical guidelines, rather than rigid adherence [2,6].

Limitations

This study has several limitations. Its retrospective design restricts causal inference and introduces the potential for selection and reporting bias. Additionally, data on patient-reported outcomes—such as postoperative quality of life or time to return to normal activity—were unavailable. Surgeon experience level, which likely influenced both technique selection and outcomes, was inconsistently documented and could not be reliably included in the analysis.

Conclusion

This study demonstrates that adherence to the 2018 EHS guidelines in inguinal hernia repair is variable, even within a high-volume tertiary care setting. Although approximately 60% of procedures were guideline-conforming, clinical outcomes such as recurrence and chronic postoperative pain did not differ significantly between conforming and non-conforming surgeries. However, the increased rate of wound-related complications associated with the TAPP technique underscores the importance of context-aware surgical decision-making.

Overall, our findings support the view that while clinical guidelines serve as a valuable framework, real-world surgical care must accommodate a variety of practical considerations, including patient characteristics, institutional resources, and surgeon expertise. Future revisions of the EHS guidelines should integrate these contextual factors to enhance their applicability and promote broader adherence in daily clinical practice.

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Cases with periodic increase: Approach to snakebites in plastic surgery

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Ethics Committee Approval
This study was approved by the Kahramanmaras Sutcu Imam University Medical Research Ethics Committee, date: June 20, 2023 and number: 05. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Snakebite injuries are common in rural areas, particularly among individuals involved in outdoor activities. In Kahramanmaras, Turkey, snakebites may be considered an occupational hazard, especially for cotton pickers.
Methods: This retrospective case series includes 20 snakebite patients who were consulted by the Department of Plastic, Reconstructive, and Aesthetic Surgery at Kahramanmaras Sutcu Imam University Hospital. Patient data were collected retrospectively between 2020 and 2022.
Results: The majority of the patients were male (60%, n = 12), while 40% (n = 8) were female. The mean age of the patients was 38.15 years. The mean D-dimer level was 16.02 units, with a range of 1.12–80 units. The mean platelet count was 175,220/µL, with a range of 65,000–325,000/µL. Upper limb involvement was the most common, observed in 65% of cases, compared to 35% with lower extremity involvement. In 60% of the cases, relaxation incisions were performed, while 40% of the patients were managed conservatively. The mean duration of ICU stay and hospitalization in the plastic surgery ward were 3.7 days and 3.55 days, respectively. Two patients developed complications other than scarring: One developed subclavian vein thrombosis, and another developed finger bone necrosis requiring amputation.
Conclusion: Snake venom contains a variety of enzymes and toxins that cause not only local tissue damage but also systemic effects. In cases of snakebite, a multidisciplinary approach is essential—beginning with field management and involving a team that includes emergency physicians, internal medicine specialists, anesthesiologists, psychiatrists, and plastic surgeons—to address both the physical and psychological needs of the patient. Importantly, early surgical consultation can help prevent severe complications.

Keywords: snake bite, compartment syndrome, fasciotomy

Introduction

Snakebite injuries are common in rural areas, particularly among individuals involved in outdoor activities. In Kahramanmaras Province, Turkey, cotton, along with corn and vines, are major agricultural crops. Many villagers work as cotton pickers, making snakebites a potential occupational hazard for both the workers and their children. Complications from snakebite injuries can include cellulitis, local gangrene, bleeding manifestations, regional lymphadenopathy, compartment syndrome, and other systemic effects [1,2].

This study is a retrospective case series of 20 patients with snakebite injuries who were referred to the Department of Plastic, Reconstructive, and Aesthetic Surgery at Kahramanmaras Sutcu Imam University Hospital, Kahramanmaras, Turkey. The aim of this study was to investigate specific risk factors, relevant biomarkers, the extent of limb involvement, duration of hospitalization in the intensive care unit (ICU) and general ward, and the incidence of secondary compartment syndrome among these patients.

Materials and methods

After obtaining ethical approval from the Kahramanmaras Sutcu Imam University Medical Research Ethics Committee (Session No: 2023/07, Decision No: 05), data from all patients who were consulted by the Plastic Surgery Department were collected retrospectively between 2020 and 2022. All procedures were conducted in accordance with the ethical standards of the Institutional Research Committee and the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from each patient prior to enrollment.

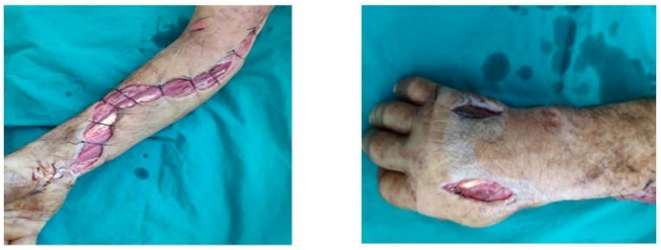
The primary assessment included measurement of vital signs and examination of the bite wound. Injury sites were cleaned and dressed with sterile gauze by emergency department physicians. All patients were evaluated for tetanus immunization status and vaccinated accordingly. Hemodynamic and biochemical parameters were closely monitored. Antivenom therapy was administered according to the Turkish Ministry of Health protocol. Patients were consulted by the Plastic Surgery Department both during initial assessment and after ICU admission. Evaluation for the need for emergency fasciotomy was primarily based on clinical examination, focusing on the six classic signs of compartment syndrome (the 6 Ps): pain, paresthesia, pallor, paralysis, perishing cold, and pulselessness, along with the ability to perform a pinch test. Notably, there were no mortalities among the patients included in this series.

Case Series

Case 1

A 63-year-old male was snake bitten in the fifth metacarpal bone of the right hand in September 2020. On presentation, platelet count was 77,000/L, and D-dimer measured 59.91 units. An emergency fasciotomy was performed (Fig. 1), and the patient was followed up in the ICU for three days. Subsequently, he was referred to the inpatient plastic surgery ward for further follow-up and reconstruction where he was hospitalized for nine days. Negative pressure wound therapy (NPWT) and approximation sutures (Fig. 1) were used to decrease wound tension before closing the wound by primary suturing.

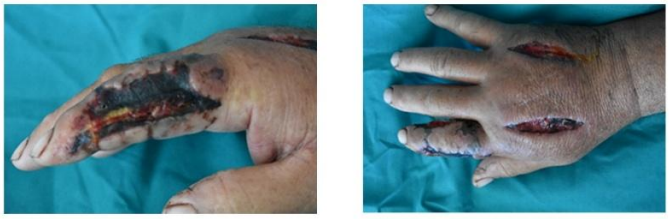
Figure 1: Snakebite in the fifth metacarpal bone of the right hand



Case 2

A 67-year-old male was snake bitten in the index finger of the right hand in August 2020. On presentation, his platelet count was 131,000/L and D-dimer measured 2.12 units. Emergency fasciotomy was performed (Fig 2), and the patient was followed up in the ICU for two days. Afterwards, he was referred to the plastic surgery ward for further follow-up and reconstruction where he was hospitalized for 11 days. He received daily paraffin dressings and tangential debridement before the wound was closed by primary suturing before discharge.

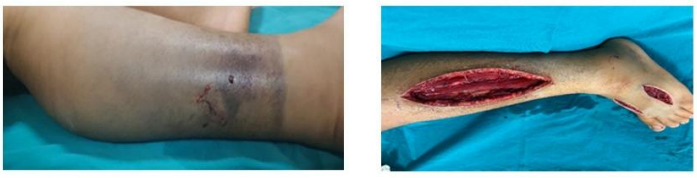
Figure 2: Snakebite in the index finger of the right hand



Case 3

An 11-year-old male was snake bitten in the medial area of the lower third distal section of the left leg in September 2020. On presentation, his platelet count was 97,000/L, and his D-dimer measured 4.74 units. Emergency fasciotomy was performed. The patient was followed up in the ICU for three days and subsequently was referred to the inpatient plastic surgery ward for further follow-up and reconstruction. He was hospitalized for ten days where NPWT and approximation sutures were used to decrease the wound tension before closing the wound by primary suturing (Figure 3).

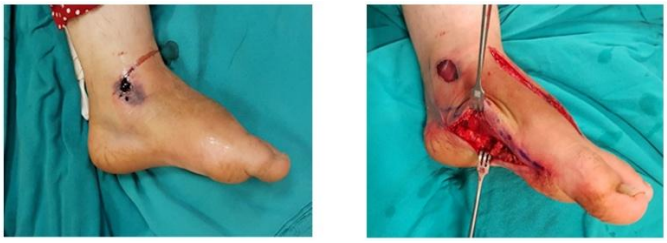
Figure 3: Snakebite in the medial aspect of the distal third section of the left leg



Case 4

A 14-year-old female was snake bitten in her left medial malleolus in August 2020. On presentation, her platelet count was 135,000/L, and her D-dimer measured 11.06 units. Emergency fasciotomy was performed, and the patient was followed up in the ICU for 13 days. She was then referred to the inpatient plastic surgery ward for further follow-up and reconstruction where she was hospitalized for four days. NPWT was used to decrease wound tension before closing the wound by primary suturing (Figure 4).

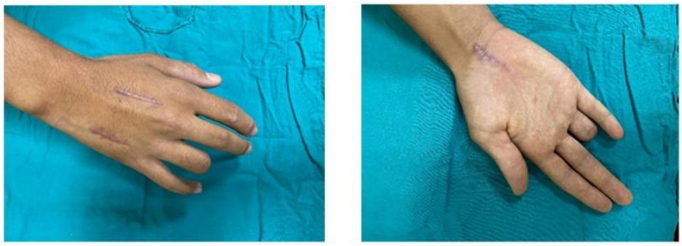
Figure 4: Snakebite in the left medial malleolus



Case 5

A 14-year-old male was snake bitten on the ring finger of the right hand in July 2020. On presentation, his platelet count was 216,000/L, and his D-dimer measured 2.10 units. Emergency fasciotomy was performed. The patient was followed up in the ICU for seven days and then referred to the inpatient plastic surgery ward for further follow-up and reconstruction. Total necrosis of the intermediate and distal phalanges was detected and amputation was performed; one day later he was discharged (Figure 5).

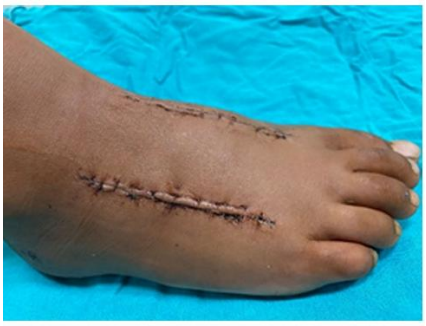
Figure 5: Snakebite in the ring finger of the right hand



Case 6

A 13-year-old male was snake bitten in the right medial malleolus in September 2020. On presentation, his platelet count was 186,000/L, and his D-dimer measured 2.03 units. Emergency fasciotomy was performed. The patient was followed up in the ICU for six days and subsequently was referred to the inpatient plastic surgery ward for further follow-up and reconstruction where he was hospitalized for one day (Fig 6).

Figure 6: Snakebite in the right medial malleolus



Results

According to the data collected from our sample, the majority of patients were male (60%), while 40% were female. The mean age of the 20 patients was 38.15 years (SD: 23.69). Adult patients outnumbered pediatric patients (Chart 1).

The mean D-dimer level was 16.02 units (SD: 24.23); two patients were excluded from this calculation due to missing or invalid data. The mean platelet count was 175,220/µL (SD: 70,140). Thrombocytopenia, defined as a platelet count below 150,000/µL [2], was present in eight patients upon admission.

Upper limb involvement was more common than lower limb involvement (65% vs. 35%). Relaxation incisions were performed in 60% of cases, while the remaining 40% were managed conservatively (Chart 2).

The mean duration of ICU hospitalization was 3.7 days (SD: 2.77), and the mean length of stay in the plastic surgery ward was 3.55 days (SD: 5.00). Details, including case number, age, gender, affected limb, presence of relaxation incision, complications, and month of presentation, are summarized in Table 1. The highest number of cases occurred in August, with most cases presenting during the summer and autumn months (Chart 3). It is important to note that only descriptive statistics were applied in this analysis; no formal statistical comparisons were conducted.

Chart 1: The proportion of age groups

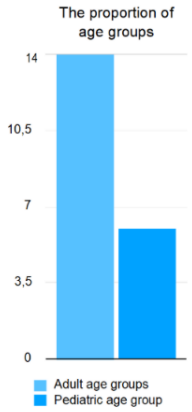


Chart 2: Treatment approach of cases

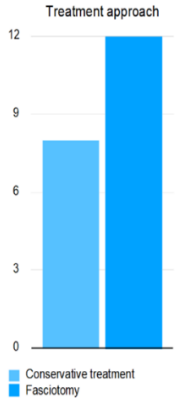
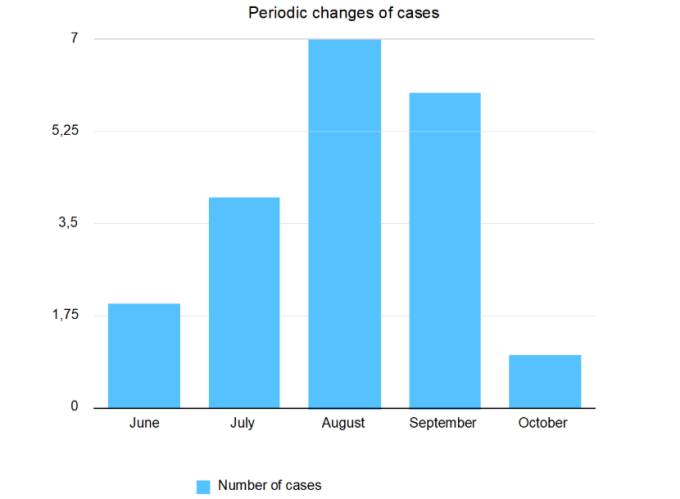


Table 1: Details about cases

Case no	Age	Gender	Affected limb	Treatment method	Additional intervention	Month	Complication
1	63	male	Upper extremity	Relaxation incision	NPWT followed by primary closure	Sept 2020	None
2	67	male	Upper extremity	Relaxation incision	Necrotic tissue debridement followed by primary closure	Aug 2020	None
3	35	female	Upper extremity	Relaxation incision	Necrotic tissue debridement followed by primary closure	Aug 2020	None
4	49	female	Upper extremity	Relaxation incision	Primary closure	Sept 2020	Subclavian vein thrombosis
5	11	male	Lower extremity	Relaxation incision	NPWT and approximation sutures followed by primary closure	Sept 2020	None
6	14	male	Upper extremity	Relaxation incision	Primary closure	Aug 2021	None
7	14	female	Lower extremity	Relaxation incision	NPWT followed by primary closure	Aug 2020	None
8	14	male	Upper extremity	Relaxation incision	Finger amputation	July 2020	Finger amputation
9	92	female	Upper extremity	Relaxation incision	Primary closure	Aug 2021	None
10	13	male	Lower extremity	Relaxation incision	Primary closure	Sept 2020	None
11	42	male	Upper extremity	Conservative follow- up	PRF	July 2021	None
12	42	female	Upper extremity	Conservative follow- up	Necrotic tissue debridement, NPWT,PRF followed by reconstruction with ingunal flap	Sept 2021	None
13	47	male	Upper extremity	Relaxation incision	polyhexanid gel dressings followed by primary closure	Oct 2021	None
14	62	female	Lower extremity	Conservative follow- up	polyhexanid gel dressings	July 2022	None
15	3	female	Lower extremity	Relaxation incision	Primary closure	Aug 2022	None
16	24	male	Upper extremity	Conservative follow- up	polyhexanid gel dressings	June 2022	None
17	19	female	Lower extremity	Conservative follow- up	polyhexanid gel dressings	July 2022	None
18	42	male	Upper extremity	Conservative follow- up	polyhexanid gel dressings	Aug 2022	None
19	57	male	Lower extremity	Conservative follow- up	polyhexanid gel dressings	Sept 2022	None
20	53	male	Upper extremity	Conservative follow- up	polyhexanid gel dressings	June 2022	None

Chart 3: Periodic changes of cases



Discussion

In Kahramanmaras Province, the number of snakebites reported to our clinic is likely lower than the actual incidence, as many individuals initially opt for traditional remedies before seeking medical care. In the present case series, we report 20 snakebite cases referred to the Plastic Surgery Department.

Montivipera albizona is a mountain viper endemic to Kahramanmaras, which was first described by Nilson et al. (1990; originally as Vipera albizona) based on two specimens from the Kulmac Mountain Range, near the "Anatolian Diagonal" [1]. However, identifying the snake species in bite cases is often not feasible, so all bites should be managed as venomous due to the high potential for serious complications.

Snakebites primarily affect the working population in rural areas, with children and the elderly at higher risk of mortality. Nevertheless, such incidents have been increasingly reported in developed regions as outdoor leisure activities become more popular [2]. Snakebites typically involve the extremities, with upper limbs more commonly affected than lower limbs [3].

Once venom is injected, patients may experience intense pain, numbness, swelling, and hemolysis in the affected limb. Significant swelling can cause vascular compression, potentially leading to compartment syndrome. The capillary leak induced by venom results in plasma and red blood cell extravasation, causing ecchymosis and tissue edema. Although various classification systems for snakebites are commonly used in emergency departments for initial evaluation, a standardized algorithm specifically guiding fasciotomy decisions is lacking [4]. In this study, we aimed to investigate potential risk factors, relevant biomarkers, the extent of limb involvement, durations of ICU and ward stays, and the proportion of patients who developed secondary compartment syndrome.

In adults compartment pressure higher than 40 mmHg is considered a clear indication for surgical intervention [2]. When pressure measurement is unavailable, clinical signs of compartment syndrome remain the best guide, though ischemic signs—aside from severe pain—are considered late indicators and should not delay the intervention [5]. If left untreated, compartment syndrome can lead to neurovascular compromise, tissue necrosis, and may ultimately result in limb amputation or, in severe cases, death [6].

Systemic and local complications of snakebites can include acute kidney injury, osteomyelitis, myositis, chronic wound infections, muscle and tendon contractures, and physical deformities that may require reconstructive surgery. In our series, one patient developed subclavian vein thrombosis, and another developed necrosis of the intermediate and distal phalanges, resulting in amputation [7,8]. Korambayil et al. [9] described three tissue zones at the bite site: a central zone of envenomation with potentially irreversible damage, an intermediate zone where tissue may recover if inflammation is controlled, and an outer zone of minimally injured tissue susceptible to secondary damage.

Previously, wound incisions and suction were believed to help remove venom, but current evidence shows that this approach worsens patient outcomes, and it is no longer recommended [10]. Instead, relaxation incisions can aid in pressure relief and venom drainage, enhancing lymphatic and venous return; in our series, relaxation incisions were performed in 60% of cases [5]. Empirical antibiotic therapy—such as a combination of amoxicillin/clavulanate and ciprofloxacin—is recommended to reduce infection-related complications [10,11]. Postoperative healing may be improved with adjunctive treatments like negative pressure wound therapy (NPWT), hyperbaric oxygen therapy (HBO), and platelet-rich fibrin (PRF) [9]. Once compartment pressures normalize, wound closure can be achieved through primary suturing or reconstructive techniques.

Conclusion

In conclusion, snakebite incidents peak during the summer season, particularly in August. The majority of affected individuals are adults, with males being predominantly affected—likely due to the occupational and outdoor activities common in the Eastern Mediterranean population. Snake venom components cause not only local tissue destruction but also systemic effects. Therefore, effective management of snakebites requires a multidisciplinary approach, starting with pre-hospital care and continuing through specialized hospital treatment. Care teams should ideally include emergency physicians, internists, anesthesiologists, psychiatrists, and plastic surgeons to address both physical and psychological consequences. Importantly, early surgical consultation can help prevent serious complications.

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Hypovitaminosis D and linkages to sleep and fatigue in Turkish patients with and without rheumatoid arthritis

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Ethics Committee Approval
The study was approved by the inical Research Ethics Committee of Gaziosmanpaşa Training and Research Hospital (Date: February 5, 2020, No: 30).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: We investigated Vitamin D levels in Turkish patients with and without rheumatoid arthritis (RA) to examine relationships with disease activity, sleep quality, sleepiness, fatigue, and physical capacity. Additionally, we evaluated the broader implications of the recent withdrawal of vitamin D testing from primary care settings.

Methods: A single-center, analytical study was conducted using laboratory records and various questionnaires: the Health Assessment Questionnaire (HAQ), Disease Activity Score (DAS-28), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), Visual Analogue Scale (VAS) for pain, and Physical Activity Questionnaire for Primary Care (PAQ-PC).

Results: A total of 192 patients were evaluated, including106 with RA that had a mean age of 53.5 (14.2) years; we also studied 86 controls that had a mean age of 49.8 (13.4) years with similar Vitamin D levels (21.02 [10.78] ng/mL vs 20.22 [8.81]) ng/mL; P=0.578). The prevalence of hypovitaminosis D was also similar across the groups (52.8% vs 48.8%; P=0.578). The Vitamin D levels of the RA patients were negatively correlated with pain (r=-0.286; P=0.033), tender joint count (r=-0.197 P=0.042), and disease activity (r=-0.286 P=0.003). In addition, RA patients exhibited poorer sleep quality and more daytime sleepiness compared with the controls; the RA patients had significantly poorer sleep quality scores (P<0.001). Similarly, the control group with hypovitaminosis D were found to have higher levels of fatigue and daytime sleepiness compared with individuals with normal Vitamin D levels (P=0.035 and P=0.019, respectively).

Conclusion: Given the high prevalence of hypovitaminosis D and its associations with disease activity, pain, fatigue, and poor sleep in patients with RA, these findings highlight the need to reconsider routine vitamin D screening in primary care, particularly for vulnerable and chronically ill populations.

Keywords: Vitamin D, fatigue, sleep, rheumatoid arthritis

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Introduction

The prevalence of Vitamin D deficiencies is increasing worldwide and has been reported to range from 20–90% in the Middle East, the United States, and Europe [1]. Additionally, roughly three quarters of patients with fatigue exhibit low Vitamin D levels [2]. Vitamin D is recognized for its critical role in calcium and bone homeostasis; however, its impacts are not limited to skeletal manifestations [1, 3]. It also confers immunomodulatory effects [3]. Low Vitamin D status is a prevalent condition that has been linked to a wide range of adverse health outcomes [4]. Consequently, Vitamin D deficiencies have been implicated in the pathogenesis of various autoimmune disorders, cardiovascular diseases, diabetes, hypertension, preeclampsia, cancer, and sleep disorders [3, 4]. Recent studies have suggested that Vitamin D status may potentially contribute to inflammatory disorders such as rheumatoid arthritis (RA) [5].

Patients with RA frequently suffer from poor sleep quality, which detrimentally impacts their overall well-being [6]. The chronic inflammation and pain associated with RA often disrupt sleep, resulting in fatigue and a heightened burden of disease [3, 6]. Research has shown that individuals with RA experience more significant sleep disturbances and lower sleep quality compared with healthy individuals [3]. Although studies have not provided conclusive evidence that Vitamin D levels have a direct impact on fatigue and sleep quality in RA patients [3, 5, 6], Vitamin D deficiencies have been linked to poor sleep quality in the general population [4]. Studies examining effects before and after Vitamin D supplementation have reported significant improvements in sleep quality. Sleep deprivation has been identified as a significant factor contributing to hyperalgesia (i.e., an increased sensitivity to pain). Recent studies have also linked Vitamin D deficiencies to both sleep disturbances and hyperalgesia, suggesting a potential interplay among sleep, pain sensitivity, and Vitamin D levels [7, 8]. Meta-analyses have indicated a significant reduction in Pittsburgh Sleep Quality Index scores for individuals receiving Vitamin D [4]. Additionally, Vitamin D deficiency has been linked to reduced muscle strength and increased disease activity in RA patients [7].

In Turkey, periodic follow-ups for pregnant women, children, and individuals with chronic diseases—groups at high risk for Vitamin D deficiencies—are typically conducted in primary care settings. Unfortunately, these primary care facilities lack the resources to measure Vitamin D levels, hindering the effective monitoring and management of Vitamin D deficiency in these vulnerable populations. A comprehensive meta-analysis, which included 40 research articles that spanned 111,582 individuals from various communities in Turkey, found that the overall prevalence of Vitamin D deficiency was around 63% [9]. This high prevalence suggests that even higher figures are expected for the Turkish population with chronic diseases.

We evaluated the prevalence of hypovitaminosis D and its correlation with RA disease activity, sleep quality, sleepiness, fatigue, and physical activity among RA patients compared with an RA-free population. We conducted this study to address the conflicting findings of previous studies in Turkey and the lack of sufficient studies on Vitamin D levels in RA patients within primary care. Furthermore, we assessed the broader implications of the recent cessation of Vitamin D testing from primary care settings in Turkey, highlighting its potential impact on patient management and clinical outcomes.

Materials and methods

Study design

This analytical case-control study was conducted with 192 subjects (106 RA patients and 86 control patients). The RA patients were selected from the Rheumatology Clinic at University of Health Sciences Gaziosmanpaşa Training and Research Hospital, (Istanbul, Turkey) provided that they had not taken Vitamin D supplements within the last three months; control cases were randomly selected from the Family Medicine Clinic at Gaziosmanpasa Training and Research Hospital (Istanbul, Turkey) from February 25, 2020 through May 15, 2020. Informed consent was obtained from the patients prior to their participation in the study. The ethics committee of the Gaziosmanpaşa Training and Research Hospital approved the study February 5, 2020 (No: 30).

A rheumatologist followed and evaluated patients with RA. Control cases included patients who visited the family medicine clinic for routine health checks or prescriptions for chronic diseases (e.g., hypertension, diabetes, asthma, chronic obstructive pulmonary disease) and who had their Vitamin D levels measured within the last three months. We excluded individuals with connective tissue diseases, endocrine disorders related to bone health (such as thyroid, parathyroid, adrenal disorders, and electrolyte imbalances), malnutrition, renal dysfunction, people receiving medications that could affect bone health (including corticosteroids, chemotherapy, anticonvulsants, diuretics, thyroxin, H2 blockers, or proton pump inhibitors), and individuals diagnosed with psychiatric disorders, dementia, or sleep disorders. Finally, we excluded anyone who was taking Vitamin D supplements.

Data Collection and Measurements

Participant data, including age, gender, Body Mass Index (BMI), education level, occupation information, income level, disease duration, comorbidity, medications currently used, rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP), 25(OH)D levels, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), complete blood count, parathormone levels, electrolytes, liver, kidney, thyroid function tests, and electrolyte values were recorded for the RA patient group. 25(OH)D levels were assessed as follows: normal Vitamin D (25(OH)D) level (30–100 ng/ml) and hypovitaminosis D (0–29.9 ng/ml) [9]. The Health Assessment Questionnaire in Rheumatic Diseases (HAQ), Disease Activity Score 28 (DAS28), Fatigue Severity Scale, Pittsburgh Sleep Quality Index (PSQI), and the Physical Activity Test Score in Primary Care were administered.

Health assessment questionnaire in rheumatic diseases

The Health Assessment Questionnaire in Rheumatic Diseases (HAQ) scale developed by Fries et al. [10] was adapted into Turkish by Küçükdeveci et al. [11]. The scale has a 4-point Likert structure, and a higher score corresponds to lower levels of health. A minimum of 0 points and a maximum of 3 points can be obtained for each question: 0 points correspond to "I can do it comfortably.", and 3 points correspond to "I can't do it at all." [10, 11].

Disease Activity Score 28

The Disease Activity Score 28 (DAS28) score, developed by Fransen et al. [12], indicates RA disease activity. The score incorporates the count of tender and swollen joints across 28 specific sites, a patient global assessment via a Visual Analogue Scale (VAS), and inflammatory markers such as Erythrocyte Sedimentation Rate (ESR) or C-Reactive Protein (CRP). The minimum score is 0, and the maximum score is 9.4. A DAS28 score less than 2.6 corresponds to remission, a score of 2.6–3.2 corresponds to mild disease, a score of 3.3–5.1 corresponds to moderate disease, and a score of greater than 5.1 corresponds to severe disease [12].

Fatigue Severity Scale

The Fatigue Severity Scale developed by Krupp et al. [13] is a 9-item, 7-point Likert-type scale (1="I completely disagree," 7="I completely agree") adapted to Turkish by Armutlu et al. [14]. The cut-off value for pathological fatigue is 4 points. As the total score decreases, the severity of fatigue decreases [13, 14].

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI), developed by Buysse et al. [15], was validated in Turkish by Agargun et al. [16]. The total score of the 7-component scale yields the PSQI value. It is a 4-point Likert-type scale with a score ranging from item 0 (no distress) to item 3 (severe distress). A total score of at least 5 points on the PSQI indicates poor sleep quality [15, 16].

Epworth Sleepiness Scale

The Epworth Sleepiness Scale (ESS) developed by Johns et al. [17] was adapted into Turkish by Ağargün et al. [18]. It is an 8-item scale that is simple to apply, easy to understand, and has proven validity and reliability in assessing general sleepiness levels in adults. A score of 6 points and above is considered sleepy. A score of 6–10 points indicates normal but increased daytime sleepiness, a score of 11–12 points indicates considered increased but moderate daytime sleepiness, a score of 13–15 points to increased, moderate daytime sleepiness, and a score of 16–24 points indicates increased and severe daytime sleepiness [17, 18].

Physical Activity Test Score in Primary Care

The Physical Activity Test Score in Primary Care scale, which was developed by Ahmad et al. [19] and consists of three subheadings and seven questions, was adapted to Turkish by Noğay et al. [20]. The first section evaluates the person's mobility at work; the second section assesses activities performed in the past seven days and the number of hours spent on them per week; and the last section includes a question evaluating the person's normal walking speed. The scale categorizes daily physical activity levels into four groups: active, moderately active, less active, and inactive [19, 20].

Statistical Analysis

Statistical analyses were performed using the e-PİCOS calculator (https://e-picos.com.tr/apps/calculation) program. The Kolmogorov-Smirnov test, skewness, and kurtosis values were applied to evaluate the normality of the data. Continuous variables were summarized using means, medians, standard deviations, and interquartile ranges; categorical variables were reported as frequencies and percentages. The chi-square test was used to compare categorical data. For quantitative data, the Independent Samples T-Test and One-Way ANOVA were used for data with a normal distribution; the Mann-Whitney U test and Kruskal-Wallis test were used for non-normally distributed data. Correlations were analyzed between Vitamin D levels and study-related parameters. Additionally, ROC (Receiver Operating Characteristic) analysis was used to determine cut-off levels for scale scores based on the presence of hypovitaminosis D.

Results

The mean age of the RA patients was 53.59 (14.2) years; the mean age of the controls without RA was 49.8 (13.4) years. As shown in Table 1, baseline characteristics, including age, gender, and BMI, were comparable between the RA and control groups; socioeconomic indicators differed significantly between the two groups. The proportions of individuals with low income, those with no education, and those who were unemployed were significantly higher than in the control group (P=0.022, P<0.001, and P<0.001, respectively).

Data pertaining to hypovitaminosis D, fatigue, sleep quality, daytime sleepiness, and physical activity between the study (RA) and control groups are listed in Table 2. Despite a similar prevalence of hypovitaminosis D in the RA and control groups (P=0.582), RA patients exhibited higher levels of fatigue (P<0.001), sleepiness (P<0.001), poorer sleep quality (P<0.001), and lower physical activity levels (P<0.001) compared with patients in the control group.

Table 1: Baseline characteristics of patient and control groups

Variables		Study (RA) group n=106	Control group n=86	*P*-value
Age, mean (SD)		53.49 (14.2)	49.8 (13.44)	[1]0.068
		n (%)	**n (%)**	
Gender	Female	83 (78.3)	61 (70.9)	[2]0.241
	Male	23 (21.7)	25 (29.1)	
Marital status	Single	16 (15.1)	17 (19.8)	[3]0.509
	Married	90 (84.9)	69 (80.2)	
Education	None	28 (26.4)	5 (5.8)	**[2]<0.001***
	Basic education	53 (50)	44 (51.2)	
	High school	15 (14.2)	18 (20.9)	
	University	10 (9.4)	19 (22.1)	
Income level	Low	70 (66)	40 (46.5)	
	Moderate	16 (15.1)	18 (20.9)	**[2]0.022***
	High	20 (18.9)	28 (32.6)	
Occupation	Unemployed	65 (61.3)	22 (25.6)	**[2]<0.001***
	Retired	18 (17)	26 (30.2)	
	Desk job	5 (4.7)	16 (18.6)	
	Physical work	18 (17)	22 (25.6)	
Comorbidity	Yes	76 (71.7)	65 (75.6)	[2]0.545
	No	30 (28.3)	21 (24.4)	
BMI, mean (SD)		28.76 (6.48)	28.48 (4.2)	[1]0.719
Number of medications, median (IQR)		2.11 (2.03) (2)	1.88 (2.02) (1)	[4]0.362

[1] Student t Test, [2] Continuity (Yates), [3] Ki-Square Test, [4] Mann Whitney U Test, * P<0.05

Table 3 lists scale scores according to the presence of hypovitaminosis D in the study (RA) and control groups. Patients with RA and low Vitamin D levels had higher DAS-28 and PSQI scores compared with the control group (P=0.040 and P=0.005, respectively). Individuals in the control group with low Vitamin D levels exhibited higher levels of fatigue and sleepiness scores (P=0.035 and P=0.019, respectively).

Table 4 lists variables related to RA, DAS-28 score, HAQ score, VAS pain score, VAS patient global score, and the number of swollen or tender joints (SJN or TJN) according to Vitamin D levels in study (RA) and control groups. We observed negative correlations between Vitamin D levels and TJN (r=-0.197; P=0.042), VAS pain score (r=-0.208; P=0.033), and DAS-28 score (r=-0.286; P=0.003).

Table 2: Evaluation of hypovitaminosis D, fatigue, sleep quality, daytime sleepiness, and physical activity between the study (RA) and control groups.

Variables		Study (RA) group n=106	Control group n=86	*P*-value
		Mean (SD) or Median (IQR)	Mean (SD) or Median (IQR)	
25(OH)D level		21.02 (10.78)	20.22 (8.81)	[1]0.578
Fatigue severity score		4.30 (3.36)	2.00 (2.00)	[2]**<0.001***
PSQI score		7.00 (5.25)	4.00 (2.00)	[2]**<0.001***
Epworth sleepiness scale score		9.00 (6.00)	6.00 (5.00)	[2]**<0.001***
Physical activity score		0.00 (1.00)	1.00 (2.00)	[2]**<0.001***
		n (%)	**n (%)**	
Vitamin D groups	Hypovitaminosis D	56 (52.8)	42 (48.8)	[3]0.582
	Normal 25(OH)D level	50 (47.2)	44 (51.2)	
Fatigue groups	No fatigue	29 (27.4)	53 (61.6)	[3]**<0.001***
	Fatigue	56 (52.8)	32 (37.2)	
	Chronic fatigue	21 (19.8)	1 (1.2)	
Presence of daytime sleepiness	No	64 (60.4)	75 (87.2)	[4]**<0.001***
	Yes	42 (39.6)	11 (12.8)	
Poor sleep	No	38 (35.8)	74 (86)	[4]**<0.001***
	Yes	68 (64.2)	12 (14)	

[1] Student t Test, [2] Mann Whitney U Test, [3]Ki-Square Test,[4] Continuity (Yates) Correction, * *P*<0.05

Table 3: Evaluation of scale scores according to vitamin D levels in study (RA) and control groups

		Vitamin D groups		*P*-value
	Scores	**Hypovitaminosis D** (n=108)	**Normal 25(OH)D level** (n=84)	
		Mean (SD) or Median (IQR)	**Mean (SD) or Median (IQR)**	
Study (RA) group	DAS-28 score (median)	3.94 (1.42)	3.43 (2.46)	[1]**0.040***
	HAQ score	28.18 (12.24)	23.98 (14.81)	[2]0.113
	Fatigue severity score (median)	4.9 (3.18)	4.00 (3.58)	[1]0.597
	PSQI score (median)	8.00 (7.00)	6.00 (4.00)	[1]**0.005***
	Epworth sleepiness scale score (median)	9.5 (6.75)	9.00 (7.00)	[1]0.473
Control group	Fatigue severity score (median)	2.95 (2.46)	1.95 (1.33)	[1]**0.035***
	PSQI score (median)	4.00 (2.25)	4.00 (1.75)	[1]0.758
	Epworth sleepiness scale score (median)	7.5 (4.00)	5.00 (4.00)	[1]**0.019***

[1] Mann Whitney U Test, [2] Student t Test, **P*<0.05, DAS: disease activity score, HAQ: health assessment questionnaire, VAS: visual analogue scale, PSQI: Pittsburgh Sleep Quality Index

Table 4: Analysis of the relationship between disease-related parameters and vitamin D levels in RA patients.

Study (RA) group (n=106)		25(OH)D level
Age of symptom onset	**r**	**-0.039**
	p	**0.691**
Age of RA diagnosis	**r**	**0.044**
	p	**0.656**
Disease duration	**r**	**0.071**
	p	**0.471**
Swollen joint count (SJC)	**r**	**-0.136**
	p	**0.165**
Tender joint count (TJC)	**r**	**-0.197**
	p	**0.042***
VAS Patient global score	**r**	**-0.185**
	p	**0.058**
VAS pain score	**r**	**-0.208**
	p	**0.033***
DAS-28 score	**r**	**-0.286**
	p	**0.003***
HAQ score	**r**	**-0.185**
	p	**0.058**

*Pearson Correlation Analysis, * P<0.05, r=Correlation co-efficient, DAS: disease activity score, HAQ: health assessment questionnaire, VAS: visual analogue scale

Table 5 lists data pertaining to Vitamin D levels and age, BMI, fatigue severity score, PSQI score, Epworth sleepiness scale score, and physical activity score. In the RA group, higher vitamin D levels were associated with a decrease in PSQI scores, which indicates better sleep quality (r=-0.205; *P*=0.035). In the control group, Vitamin D levels were negatively correlated with age (r=-0.226; *P*=0.037), fatigue severity (r=-0.254; *P*=0.018), and daytime sleepiness (r=-0.285; *P*=0.008).

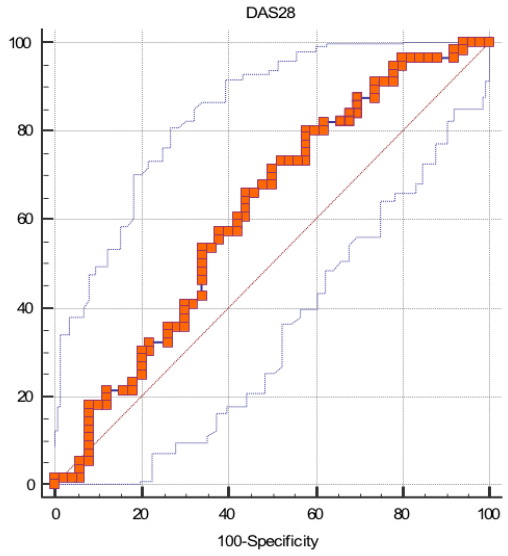
Table 5: Relationship between vitamin D level and age, BMI, fatigue severity score, PSQI score, Epworth sleepiness scale score and physical activity score

		25(OH)D level		
		All (n=192)	**Study (RA) group (n=106)**	**Control group (n=86)**
Age	**r**	-0.046	0.057	***-0.226***
	p	0.527	0.562	***0.037****
BMI	**r**	-0.024	-0.038	**0.007**
	p	0.745	0.696	**0.949**
Fatigue severity score	**r**	-0.111	-0.087	***-0.254***
	p	0.127	0.375	***0.018****
PSQI score	**r**	-0.131	*-0.205*	**-0.117**
	p	0.071	***0.035****	**0.283**
Epworth sleepiness scale score	**r**	*-0.166*	-0.137	***-0.285***
	p	0.022*	0.161	**0.008***
Physical activity score	**r**	-0.010	0.038	**-0.042**
	p	**0.894**	**0.697**	**0.700**

Pearson Correlation Analysis, * *P*<0.05, r: Correlation co-efficient, PSQI: Pittsburgh Sleep Quality Index, BMI: Body Mass Index

Figure 1 shows the ROC (Receiver Operating Characteristic) curve for DAS-28 score in the presence of hypovitaminosis D. The cutoff point determined for DAS-28 was 3.03 in corresponding to low disease activity (2.6–3.2) according to EULAR criteria. The sensitivity of this value was found to be 80.4%, with a specificity of 42.0%. The positive predictive value was 60.8%, and the negative predictive value was 65.6%. Clinically, these results indicate that RA patients with a DAS-28 activity score of 3.03 (i.e., exhibiting moderate to severe disease activity), are likely to have hypovitaminosis D (*P*=0.037).

Figure 1: ROC curve for DAS-28 in the diagnosis of hypovitaminosis D



Discussion

We assessed the relationship between Vitamin D levels and various health parameters in RA patients, including disease activity, sleep quality, fatigue severity, and physical activity levels. We then made comparisons with a control group. Hypovitaminosis D was noted in 52.8% of RA patients and 48.8% of control group patients. Our findings revealed that RA patients with hypovitaminosis D experienced significantly poorer sleep quality and had more fatigue and daytime sleepiness than the control patients. Notably, all RA patients with moderate to severe DAS-28 disease activity require Vitamin D supplementation. Similarly, control group patients with hypovitaminosis D were found to have higher levels of fatigue and daytime sleepiness compared to individuals with normal Vitamin D levels. These findings highlight the association between Vitamin D levels and parameters such as sleep and fatigue.

In Turkey, the Ministry of Health has implemented new regulations to address the significant increase in Vitamin D testing that began in 2019. These regulations are intended to optimize testing and reduce unnecessary demand. The relevant measures include removing Vitamin D testing in primary care facilities and limiting the service in secondary and tertiary care settings to specific specialists, such as pediatricians, internists, obstetricians, physiatrists, orthopedists, and neurologists. A mandatory 90-day interval has been introduced for repeat tests, but exceptions are made for inpatients and intensive care patients. In emergency departments, test requests are similarly restricted to the specialists noted above. These changes are intended to conserve resources and ensure that Vitamin D testing is prioritized for patients with clear clinical indications.

However, in primary care Vitamin D levels are critical for monitoring chronic diseases, the health of women aged 15-49, geriatric patients, pregnant women, and children. Requiring every patient with specific needs to consult a specialist may not be practical for Vitamin D testing. Many studies of RA have reported that more women than men are afflicted by the disease [21]. For instance, Grabovac et al. [22] showed that 32.6% of RA patients were male, while 67.4% were female. Our study is consistent with this trend, with 78.3% of the participants being female and 22.7% being male.

Although no prior studies have linked low income with the prevalence of RA, our findings showed that Vitamin D deficiencies were more prevalent among RA patients with low socioeconomic status. This finding suggests that financial barriers may contribute to Vitamin D deficiencies in this population. But in healthcare systems where primary care services—including laboratory testing and examinations—are provided free of charge, income level may no longer be a limiting factor when it comes to monitoring and replacing Vitamin D. That situation only holds true, however, provided that Vitamin D testing is available at the primary care level.

In addition, low Vitamin D levels have been associated with an increased risk of developing RA and are linked to higher RA disease activity and poorer general health status [23]. A 2016 meta-analysis of 15 studies that encompassed 1,143 RA patients and 963 controls found significantly lower Vitamin D levels in RA patients; Vitamin D levels were inversely correlated with RA disease activity [24]. Another meta-analysis of 3,489 patients reported a similar inverse correlation between low Vitamin D levels and disease activity [25]. A 2020 meta-analysis showed that VAS scores significantly decreased in patients taking at least 50,000 IU of Vitamin D supplements per week for at least 12 weeks; patients in that group also exhibited a reduction in DAS-28 activity scores. No changes were observed in patients who took less than 50,000 IU of Vitamin D per week or followed that regime for less than 12 weeks [26]. In a 2017 randomized, double-blind, placebo-controlled study with 39 RA and 31 control patients, new-onset RA patients who received 300,000 IU of 1.25 dihydroxy cholecalciferol exhibited significantly better general health assessments after three months compared with patients in the placebo group [27]. Another controlled trial of 121 new-onset RA patients compared patients receiving only DMARDs (Disease-Modifying Antirheumatic Drugs) with patients also receiving 500 IU of Vitamin D daily. After three months, patients in the Vitamin D group reported significantly decreased pain, but no relationship was noted between Vitamin D levels and DAS-28 scores [28]. Di Franco et al. [29] showed that in patients with new-onset RA and low Vitamin D levels, disease activity reduction, remission rates, and treatment responses were notably lower after 12 months compared with patients with normal Vitamin D levels. This result highlights the role of Vitamin D in modulating RA and suggests that assessing and supplementing Vitamin D might improve the management of new-onset RA.

In our study, Vitamin D levels were inversely correlated with pain, tender joint count, and disease activity. Patients with RA with low Vitamin D levels exhibited significantly higher disease activity. The cut-off point for DAS-28 in hypovitaminosis D was determined to be 3.03. Clinically, this result indicates that RA patients with a DAS-28 activity score of 3.03 or above are likely Vitamin D deficient. According to the RA disease activity classification of our study cohort, Vitamin D levels in cases of moderate and severe disease activity require supplementation. The VAS pain scores of patients in our RA group were negatively correlated with Vitamin D levels, a finding that is consistent with that reported in the literature [22, 24, 25].

Low levels of Vitamin D are one factor influencing fatigue during inflammatory rheumatisms [30]. In a 2014 study by Oy et al. conducted in the United States, the authors found that fatigue severity in individuals with Vitamin D deficiencies decreased after Vitamin D supplementation [31]. Patients with RA may suffer from poor sleep quality, which is attributed to depression, fatiguability, disability and disease activity [32]. In our control group, patients with sufficient Vitamin D levels had significantly lower fatigue severity compared with patients with insufficient Vitamin D levels; this finding is consistent with the literature [30, 31]. However, the Vitamin D levels of RA patients in our study did not correlate with fatigue severity, unlike in the control group.

A 2018 meta-analysis by Gao et al. [33] linked Vitamin D deficiencies with an increased risk of sleep disorders and decreased sleep quality. Similarly, Sarıyıldız et al. [34] used the PSQI scale and found that RA patients had lower sleep quality than patients in their control group; this team primarily associated low sleep quality with high RA disease activity . A review of non-pharmacological methods for relieving fatigue in RA patients demonstrated that physical activity positively impacted fatigue levels [35]. Exercise is known to improve sleep disorders in patients with RA [36]. Despite studies suggesting that all patients should exercise and take supplements to prevent muscle mass loss, Vitamin D supplementation, with or without exercise, did not significantly affect other aspects of body composition or metabolic health outcomes [37]. On the other hand, a population-based study by Mirzaei-Azandaryani et al. [38] found that sleep quality significantly improved in patients receiving Vitamin D compared with patients in the control group. In summary, higher PSQI scores—indicating poorer sleep quality—were observed in individuals with low vitamin D levels compared to those with normal levels, in both the RA and control groups.

Limitations

One limitation of this study is that a fatigue assessment may lack objectivity when it is solely based on scale scores; fatigue can be influenced by poor sleep quality or can occur

independently of sleep issues. Additionally, seasonal effects may have influenced our findings—this study began in February and concluded in May; that cycle potentially affected Vitamin D synthesis and measurement levels: Vitamin D levels are often lowest in March, as cutaneous synthesis is limited due to the angle of sunlight during the winter months [39]. We recommend conducting additional research with larger sample sizes and including Vitamin D replacement interventions to obtain more generalizable results.

Conclusions

Patients with RA and hypovitaminosis D are more fatigued and sleepy, have poorer sleep quality, and exhibit a larger number of swollen and tender joints compared with those with normal vitamin D levels.

Routine follow-ups for populations at a high risk of Vitamin D deficiencies—including pregnant women, children, the elderly, and individuals with chronic diseases—are typically conducted in primary care settings. However, the lack of resources to measure Vitamin D levels in these facilities hampers effective monitoring and management of Vitamin D deficiencies in these vulnerable groups.

Monitoring Vitamin D status during primary care follow-up for patients with chronic diseases, such as RA, is paramount for optimizing long-term clinical outcomes. We strongly advocate for the reinstatement of routine annual Vitamin D screening in primary care settings, especially for at-risk populations. In light of these findings, the broader contribution of micronutrients to health maintenance and disease prevention necessitates a thorough re-evaluation.

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Brain drain in Türkiye's nursing workforce: A literature review

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Abstract

Nurses represent the largest workforce group forming the foundation of global health systems. Despite this central role, a critical worldwide nursing shortage persists, posing significant threats to the sustainability of health systems, particularly in low- and middle-income countries. Although Türkiye's nursing workforce has expanded in recent years, it remains far below OECD (Organization for Economic Co-operation and Development) averages and struggles to meet the growing demand for healthcare services. This review adopts a comprehensive approach to examine the economic, organizational, social, and psychological factors accelerating nurse brain drain from Türkiye, drawing on national and international data. Findings indicate that low wages, heavy workloads, insufficient staffing, workplace violence, limited career opportunities, and burnout serve as major push factors influencing nurses' decision to migrate. Conversely, high-income countries such as Germany, the Netherlands, Canada, and the United Kingdom offer strong pull factors including higher salaries, safer working environments, lower nurse-to-patient ratios, and well-developed professional career pathways. While Türkiye's migration patterns share similarities with nurse-exporting countries such as the Philippines and India, high rates of workplace violence and the emigration of experienced nurses place Türkiye in a distinct position. Nurse brain drain has immediate consequences, including increased workload and negative impacts on patient safety, and long-term effects such as loss of institutional memory and transfer of educational investments to receiving countries. This review underscores the need for policy development addressing the structural drivers of nurse brain drain and provides a critical situational analysis for the future of Türkiye's healthcare system.

Keywords: nurse brain drain, pull factor, push factor

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Introduction

Nurses constitute the backbone of health systems and represent the largest professional group ensuring the continuity of healthcare delivery. According to the WHO's global report, nurses make up approximately 59% of the global health workforce, and there is an estimated global shortage of 5.9 million nurses [1]. This shortage became more visible during the COVID-19 pandemic, and competition for qualified nurses among countries has increased markedly [2, 3]. Although the nursing workforce in Türkiye has grown numerically, the country remains far behind in international comparisons. According to OECD (Organization for Economic Co-operation and Development) data, the number of nurses per 1,000 population in Türkiye is 2.9, whereas the OECD average is 9.2 [4]. Based on these figures, it can be estimated that more than 500,000 additional nurses would need to be employed in Türkiye to reach the OECD average. This numerical imbalance increases nurses' workload, fuels burnout, and accelerates workforce attrition [5, 6].

In recent years, nurse brain drain from Türkiye has risen markedly. The increase in equivalency and licensing applications submitted for working abroad further supports this trend. Notably, applications from nurses and healthcare workers to Germany have shown a significant rise [7]. Studies conducted in Türkiye also indicate that the idea of working abroad is widely supported among nurses. In field research conducted by the Turkish Nurses Association (THD), 76.3% of nurses reported that they were considering going abroad, while 21.8% stated that they had already initiated the application process [8, 9]. The aim of this review is to analyze nurse brain drain in Türkiye from economic, professional, organizational, and social perspectives; to evaluate current trends in light of the international literature; and to discuss its short- and long-term implications for the Turkish healthcare system. This analysis specifically examines the push and pull factors driving migration, compares Turkish trends with international patterns, and evaluates the systemic impacts on healthcare delivery.

What are the push factors in Türkiye and the pull factors abroad that increase nurses' brain drain tendencies?

Economy

The insufficiency of nurses' salaries in Türkiye relative to the cost of living constitutes a major economic push factor frequently emphasized in the migration literature [9, 10]. Existing studies show that most nurses believe their wages are not commensurate with their professional responsibilities, workload, and working conditions. Consequently, they describe sustainable economic well-being within the profession as increasingly difficult to maintain [11, 12]. In contrast, higher salaries, more comprehensive social benefits, and greater employment stability in high-income countries transform these destinations into strong pull factors for nurses from Türkiye [13, 14]. The literature particularly highlights expectations of economic improvement, social security provisions, and institutional support mechanisms as central pull factors shaping nurse brain drain from Türkiye [10, 15]. Collectively, these findings demonstrate that economic conditions are among the most critical determinants influencing nurses' willingness to work abroad.

Workload and staffing levels

Approximately 350,000 nurses currently work in Türkiye; however, OECD standards suggest that the country requires between 400,000 and 450,000 nurses to meet population needs [4, 16]. This deficit results in nurse-to-patient ratios far above OECD norms, leading nurses to work under excessive workload. As a consequence, nurses are often responsible for caring for more patients than recommended by international standards, which contributes substantially to burnout [6]. High workload and chronic understaffing diminish motivation and drive nurses to seek better working conditions elsewhere.

In the study by Nantsupawat et al. [17], emotional exhaustion was identified in 35.7% of nurses, depersonalisation in 29.9%, and reduced personal accomplishment in 48.2%; moreover, 9.14% of nurses reported an intention to leave their current job. Insufficient managerial support further decreases job satisfaction and increases migration intentions [18, 19]. Daşbilek et al. [20] reported that shift-based work heightens work-family conflict and burnout. Heavy workloads, intense shift demands, and inadequate staffing ratios represent some of the strongest predictors of emotional exhaustion [6, 19]. These suboptimal working conditions function as structural push factors reinforcing nurses' decisions to migrate [21, 22].

Among international pull factors, low nurse-to-patient ratios stand out. For example, in countries such as the Netherlands, Switzerland, and Sweden, a nurse typically cares for an average of 5 patients, whereas in Poland, Spain, and Germany the ratio is roughly 10 patients [23, 24]. Compared with Türkiye, these lower ratios translate into reduced stress and higher job satisfaction for nurses [5, 19]. Additionally, the ability to provide higher-quality care under manageable workloads enhances professional fulfilment and clinical efficiency.

Career opportunities

Although advanced nursing roles and career pathways are defined by regulation in Türkiye, these structures have not been effectively implemented across many healthcare institutions [11, 12]. Research among nursing students shows that access to better specialization and academic development opportunities abroad accounts for approximately 50% of the motivation to consider migration [12]. These findings highlight the extent to which structural limitations within Türkiye systematically contribute to nurse brain drain.

Conversely, professional autonomy and robust career advancement prospects serve as strong pull factors abroad. In the United States, for instance, nursing practice is supported by comprehensive regulatory and professional frameworks that grant nurses a higher degree of clinical autonomy. Similarly, the United Kingdom and Canada have expanded educational supports and professional development structures for nurses [25, 26]. The recognition of advanced nursing roles such as nurse practitioners and clinical nurse specialists provides substantial opportunities for career progression [12, 14]. These enhanced career prospects make foreign countries particularly attractive to nurses from Türkiye, many of whom believe they can access superior training and specialization pathways abroad.

Workplace safety

High rates of workplace violence in Türkiye negatively affect the work environment for nurses [11, 27]. In research

conducted by the THD, 25.8% of nurses identified exposure to psychological or physical violence as a factor influencing their intention to migrate. Nurses who experienced violence reported that these incidents strengthened their desire to work abroad [8, 9, 12]. Such experiences undermine nurses' sense of safety, rendering their workplaces insecure and eroding professional commitment. Safety deficiencies therefore operate as a significant push factor directing nurses toward countries that provide safer working environments. Safer physical and psychological working conditions in destination countries serve as a notable pull factor [28]. Countries with more robust workplace safety regulations and lower rates of violence offer particularly attractive environments for nurses from Türkiye [15, 29].

In what ways does nurse brain drain from Türkiye resemble or differ from international patterns of nurse mobility?

Similarities

Türkiye's nurse brain drain pattern shares several characteristics with major nurse-exporting countries such as the Philippines, India, and certain African nations. In these contexts, economic motivations, excessive workload, and limited career opportunities similarly emerge as primary determinants of migration [1, 10, 30, 31].

Differences

However, several critical distinctions set Türkiye apart from other nurse-sending countries. First, the high prevalence of workplace violence in the Turkish healthcare system places Türkiye in a more vulnerable position compared with many other countries [9, 11]. Second, a substantial proportion of nurses emigrating from Türkiye have 6–10 years of professional experience, contrasting with countries such as the Philippines, which predominantly send newly graduated nurses abroad [11, 12]. Third, despite the expansion of nursing education quotas in recent years, migration rates have not decreased [32]. This pattern suggests that increased training capacity alone is insufficient to curb migration unless working conditions are simultaneously improved.

What are the short- and long-term effects of nurse brain drain on the Turkish healthcare system?

Short-term effects

Short-term consequences of nurse brain drain include a worsening nursing shortage, increased workload, compromised care quality, and deterioration in patient safety indicators [23, 33]. The already substantial nursing deficit in Türkiye has been associated with longer waiting times in health facilities and declining safety metrics, largely driven by excessive nurse workload [5, 9]. As remaining nurses face even heavier burdens, burnout levels rise further, perpetuating a self-reinforcing cycle of workforce loss [6, 19].

Long-term effects

In the long term, nurse brain drain contributes to the erosion of institutional memory, a decline in experienced clinical personnel, and more challenging working environments for newly graduated nurses. Additionally, the public investment made in nursing education is effectively transferred to receiving countries when trained professionals migrate [10, 34]. The substantial financial cost required to educate a nursing student in Türkiye thus represents a significant economic loss when that nurse ultimately joins a foreign workforce.

Conclusion

This review demonstrates that nurse brain drain from Türkiye is increasing rapidly at the intersection of economic, organizational, and psychosocial factors, representing a critical threat to the sustainability of the healthcare system. Low salaries, heavy workload, widespread workplace violence, limited career advancement opportunities, and insufficient managerial support represent the primary push factors driving migration [9, 12, 17]. Conversely, high income, safer work environments, lower nurse-to-patient ratios, and well-developed career ladders in destination countries serve as strong pull factors, particularly for young and mid-career nurses [5, 10, 15].

If current trends persist, Türkiye is expected to face serious challenges in maintaining both the capacity of its nursing workforce and the quality of healthcare delivery. Improving salary policies, enhancing working conditions, strengthening legal and administrative mechanisms to prevent workplace violence, implementing advanced nursing roles, and aligning nurse-to-patient ratios with scientific standards emerge as essential strategies [18, 22, 35]. Ultimately, the retention of the nursing workforce must be prioritized as a matter of national health security rather than a mere administrative challenge. A genuine transformation in the professional status of nurses, supported by both legislative protection and institutional respect, is the only sustainable way to prevent the collapse of the domestic healthcare foundation and ensure high-quality patient care for future generations.

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Case report
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A rare congenital anomaly of the bile duct: Gallbladder agenesis

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Abstract

Gallbladder agenesis (GA) is a very rare biliary tract anomaly. Between 50% and 70% of patients are asymptomatic. It is usually diagnosed during the radiological examination of patients with dyspeptic complaints or during the operation. In this study, a 55-year-old female patient presented at our clinic for dyspepsia and was diagnosed with gallbladder agenesis. The patient was admitted to the clinic with complaints of epigastric pain, which did not correspond with times of fasting or fullness. There was no disease or complaint in the patient's history. Cholestasis enzymes, bilirubin and other laboratory values were normal. Abdominal ultrasonography (US) performed with the preliminary diagnosis of cholelithiasis revealed that there was no gallbladder. Gallbladder agenesis was detected in the magnetic resonance cholangiopancreatography (MRCP) examination. The patient was followed up and no surgical intervention was performed. The possibility of other bile duct anomalies, such as choledochal cysts and stones is high in patients with GA. These anomalies can be confused with the gallbladder in abdominal US. The risk of injury to the biliary tract, small intestine, hepatic artery, and portal vein is higher as a result of additional dissections to find the gallbladder in surgical interventions performed in patients with GA. It may be important to keep in mind the rarity of gallbladder agenesis in order to avoid unnecessary surgical interventions, such as laparoscopy and laparotomy, for patients presenting with signs of acute cholecystitis.

Keywords: gallbladder agenesis, magnetic resonance cholangiopancreatography, biliary tract anomaly, laparoscopy

Introduction

Gallbladder agenesis is the congenital absence of a gallbladder. This condition is a very rare congenital abnormality [1-4]. Gallbladder agenesis is symptomatic in 50% of cases, but its symptoms and signs are often varied. Sometimes the symptoms are mild, while in some cases they are more severe. The most common symptom is similar to right upper quadrant pain due to cholelithiasis and cholecystitis [5, 6]. It is generally thought that the patients is having an attack of acute cholecystitis. About one-third of cases are asymptomatic. In such patients, diagnoses are made incidentally or by autopsy. It is grouped with congenital anomalies incompatible with life in 15% of cases [7, 8]. Symptoms, such as pain in the gallbladder area, difficulty digesting fatty foods, and digestive problems, especially abdominal pain, bloating, gas, and diarrhea, may occur. Other problems, such as gallstones, and narrowing or blockage of the biliary tract may occur [6]. These abnormalities may be observed in liver function tests, but usually, methods including medical imaging tests, blood tests, and sometimes endoscopic examinations are used to make a diagnosis. Gallbladder agenesis can be genetic, and in some cases, family history and genetic mutations have been associated with this condition; however, to date there is not a definitive understanding of exactly how it occurs and why it occurs in some individuals. In the past, the diagnosis of gallbladder agenesis was usually made preoperatively. Currently, a magnetic resonance cholangiopancreatography (MRCP) examination is performed in cases where abdominal ultrasonography is suspected. MRCP can indicate gallbladder agenesis as well as ectopic gallbladders. In this study, a case with gallbladder agenesis will be presented.

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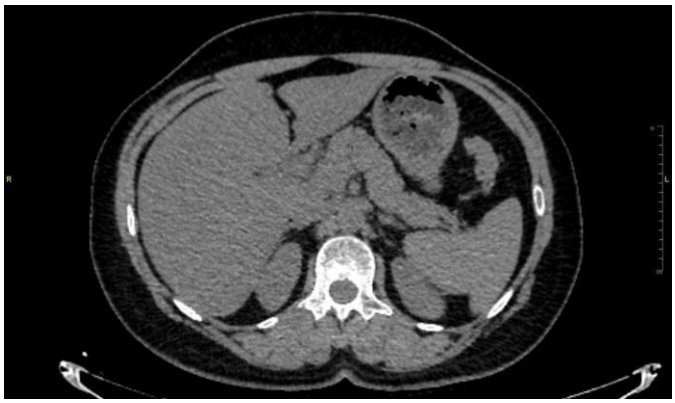
Case presentation

A 56-year-old female patient was admitted to our outpatient clinic with a complaint of pain in the epigastric region from time to time, which had been occurring for the past month. It was determined that her discomfort did not vary according to hunger or satiety, and she did not have any additional disease. Blood pressure, pulse, and body temperature were of normal values. In laboratory values, ALT, AST, GGT, ALP, amylase, lipase, total and direct bilirubin were within normal limits. The gallbladder was not visible on the upper abdominal ultrasonography examination. A computed tomographic examination of the abdomen was performed, and it was found that there was no gallbladder (Figure 1).

Figure 1: Computed Tomographic Examination of the Abdomen without Contrast.



Upper abdominal MRI and MRCP examinations were performed considering gallbladder agenesis. 3- Dimensional maximum intensity projection (MIP) reconstructions were performed in MRCP and it was found that there was gallbladder agenesis, choledochial, and intrahepatic biliary tract dilatation (Figures 2 and 3).

The patient was placed under follow-up with planned outpatient clinic controls.

Figure 2: Gallbladder agenesis in MRCP, choledochial, and intrahepatic biliary tract enlargement.

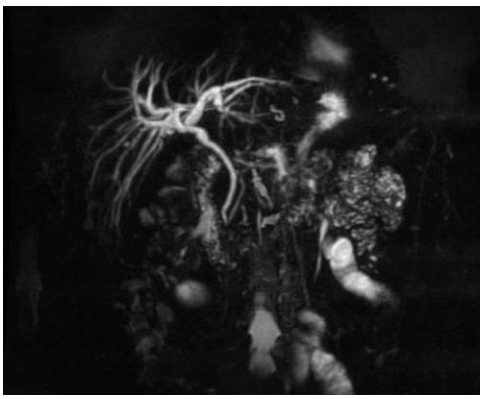
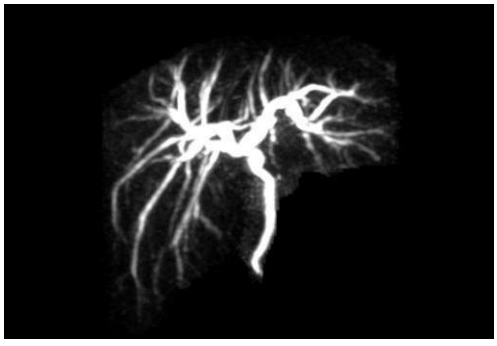


Figure 3: MRCP 3D MIP reconstruction.



Discussion

Research conducted on gallbladder agenesis and discussions in the literature are quite limited. Individuals with this condition do not usually experience symptoms, and it is often detected by chance during imaging tests. However, individuals with gallbladder agenesis may sometimes be predisposed to complications, such as gallstone formation or liver diseases. In our case, liver function tests were found to be normal in laboratory values.

Surgical interventions, such as unnecessary laparoscopy and laparotomy, can be performed on patients with a preliminary diagnosis of acute cholecystitis in symptomatic patients. Unnecessary dissections performed to locate the gallbladder during these surgical interventions may cause vascular and biliary tract injuries [7,8]. In the present case, there was a complaint of pain in the epigastric region from time to time that started in the previous month. The diagnosis of gallbladder agenesis was made by radiological examinations and an unnecessary surgical intervention was avoided.

In terms of treatment, gallbladder agenesis is usually non-symptomatic and does not require treatment. But if complications develop, for example, gallstones form or liver disease occurs, treatment methods can be applied to manage the relevant symptoms. Previous literature indicates that the diagnosis of gallbladder agenesis can be made during laparoscopy or laparotomy. It is recommended to use preoperative cholangiography and ultrasonography to confirm the diagnosis. Abdominal tomography (CT) and endoscopic retrograde cholangiopancreatography (ERCP) examinations are recommended to confirm the diagnosis [9]. With today's technological developments, the use of MR and MRCP has increased in many medical centers. This can eliminate unnecessary laparoscopy and laparotomy by making the diagnosis with MRCP, avoiding the need for surgery [2]. Although there is information in some publications that the diagnosis of gallbladder agenesis can be made by laparoscopy, today a high-tech infrastructure has been developed in many radiology clinics and MRCP examination can be performed. MRCP has superior ability to visualize the biliary tract. Therefore, unnecessary surgical interventions and possible complications can be avoided by using MRCP in cases where gallbladder agenesis is suspected in abdominal US.

It is important to keep in mind the rarity of gallbladder agenesis in order to avoid unnecessary surgical interventions, such as laparoscopy and laparotomy, for patients presenting with signs of acute cholecystitis. In addition, unnecessary dissections performed to find the gallbladder in surgical interventions ensure the avoidance of vascular and biliary tract injuries.

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Case report
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Abdominal pain post bariatric procedure: What is the cause?

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Abstract

Omental ischemia after bariatric surgery is a rare cause of abdominal pain. We report a case of a 42-year-old female with a history of Roux-en-Y gastric bypass (RYGB) presenting with abdominal pain. Despite biochemical, radiologic, and endoscopic investigation, no cause was identified. Ultimately, diagnostic laparoscopy revealed ischemic omentum. Post-operatively, her symptoms resolved. This case highlights the diagnostic challenges in patients post-RYGB presenting with abdominal pain with no clear cause. Division of the omentum is common practice during RYGB in the case of an antecolic Roux limb. This may predispose patients to omental infarction and ischemia, and as such, suspicion should be high when initial investigations are equivocal. The potential role of omental division during RYGB warrants further investigation. Furthermore, this case reinforces the importance of diagnostic laparoscopy in select cases. Rare causes of abdominal pain, such as omental ischemia, should be considered in patients who are post-RYGB. When initial investigations are negative, early diagnostic laparoscopy should be considered.

Keywords: omental infarction, omental ischemia, Roux-en-Y gastric bypass, bariatric surgery, diagnostic laparoscopy, post-operative complication

Introduction

Omental ischemia is a rare but important cause of abdominal pain in post-bariatric surgery patients. It occurs due to compromised perfusion of a portion of the omentum, resulting in ischemia, pain, and necrosis. Although it may mimic common conditions, its presentation is often nonspecific, making a diagnosis difficult without surgical exploration [1].

Here, we present a case of a patient with a history of a laparoscopic Roux-en-Y gastric bypass (RYGB) who experienced persistent abdominal pain of unclear etiology. She underwent an extensive but inconclusive diagnostic evaluation, and was ultimately found to have ischemic omentum requiring surgical intervention. This case highlights the importance of considering omental infarction in the differential diagnosis of post-RYGB abdominal pain and underscores the role of early surgical exploration in select cases.

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Informed Consent
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Case presentation

A 42-year-old female with a remote history of laparoscopic RYGB presented approximately five years postoperatively to the emergency department (ED) with a two-month history of progressively worsening right upper quadrant/epigastric pain. She described her pain as constant, focal, and sharp in the right upper quadrant and epigastrium, occasionally worsening postprandially. She has lost approximately 50 pounds since the bariatric procedure. Her past medical history included irritable bowel syndrome, acid reflux, attention deficit hyperactivity disorder (ADHD), anxiety, migraines, and restless leg syndrome. Her past surgical history included a laparoscopic appendectomy over 20 years ago, a laparoscopic cholecystectomy 12 years ago, and a cesarean section 10 years ago. Her medications included bronchodilators as needed, paroxetine, pramipexole, lisdexamfetamine, and metoclopramide as needed. She denies nonsteroidal anti-inflammatory drug (NSAID) use. She does not smoke, drink alcohol, or consume recreational drugs.

During her ED visit, no biochemical abnormalities were seen, and computed tomography (CT) of the abdomen and pelvis revealed no acute intra-abdominal abnormalities. She was discharged from the ED with prescriptions for ondansetron and a proton pump inhibitor (PPI).

Two months later, she presented with the same symptoms. On this visit, she was noted to have mild leukocytosis, elevated transaminases, as well as elevated alkaline phosphatase, gamma-glutamyl transferase, and bilirubin. These values are listed in Table 1. All other chemistries were normal, including troponin, lipase, hemoglobin, and electrolytes. A CT scan showed subtle dilatation of the intrahepatic biliary ducts, in addition to low attenuation in the falciform ligament, thought likely to be related to focal fatty infiltration, but MRI was recommended for further characterization (Figure 1, 2). She was admitted to the General Surgery service for further investigation.

The patient underwent a magnetic resonance cholangiopancreatography (MRCP), which showed subtle focal fat deposition and transient perfusion abnormality in a region of hypoattenuation near the falciform ligament, along with trace free fluid in the right upper quadrant. There was no biliary duct dilatation or cause of biliary duct dilation, such as choledocholithiasis, stricture, or mass (Figure 3).

Figure 1: Axial computed tomography scan showing subtle dilatation of the intrahepatic biliary ducts (triangle), and low attenuation in the falciform ligament (arrow).

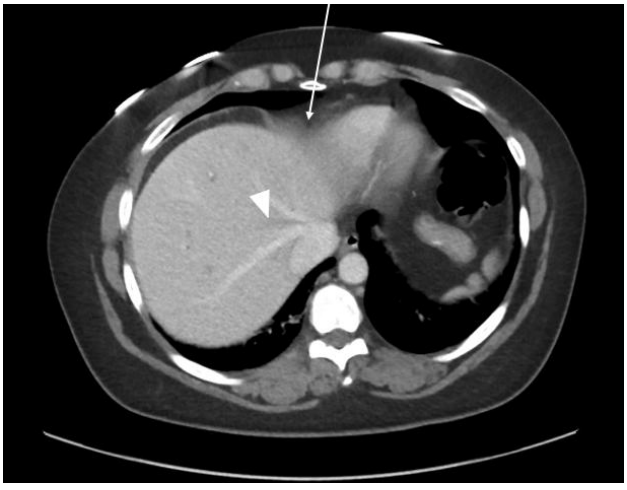


Figure 2: Sagittal computed tomography scan showing subtle dilatation of the intrahepatic biliary ducts (triangles), and low attenuation in the falciform ligament (arrow).

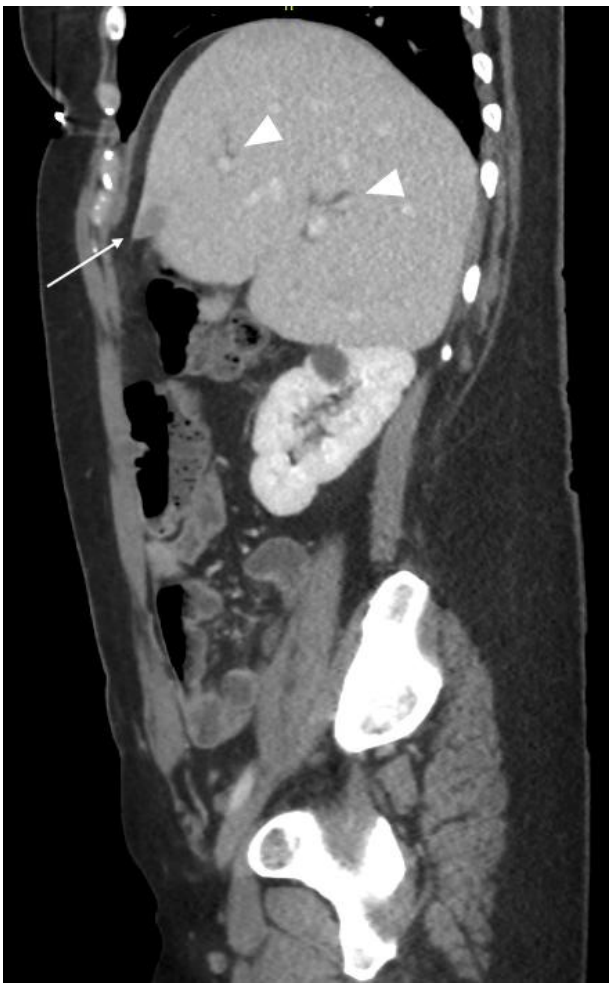
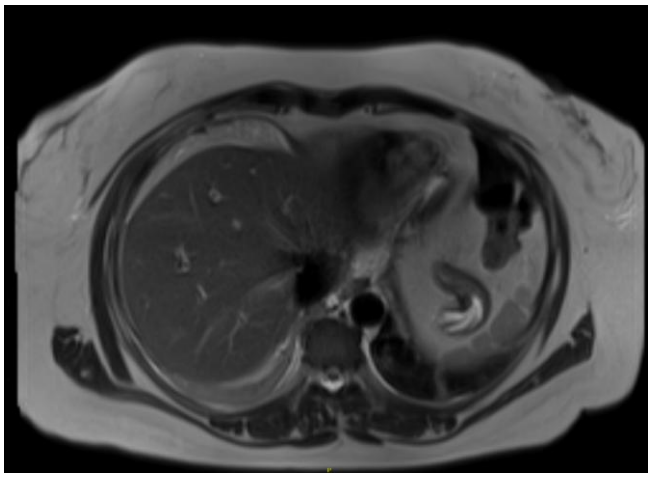


Figure 3: MRI scan showing subtle focal fat deposition, hypoattenuation near the falciform ligament (arrow), and trace free fluid in the right upper quadrant (triangle).



An esophagogastroscopy (EGD) performed on post-admission day 3 was normal; there were no ulcers, erosions, angiodysplastic lesions, or stenoses. Biopsies of the gastric pouch were taken, which revealed no *Helicobacter pylori* or dysplastic changes.

Given her ongoing symptoms and a negative workup, she underwent diagnostic laparoscopy on post-admission day 6. Intraoperatively, mildly inflamed and congested omentum was adherent to the right lobe of the liver, the right diaphragm, and the right side of the falciform ligament. This was carefully peeled off the liver with mild difficulty due to inflammatory changes, and there was diffuse mild oozing from the liver and the right diaphragm once the omentum was removed. The omentum was placed into the mid-abdomen to restore its normal anatomy and

hemostasis was achieved. A thorough diagnostic laparoscopy was performed, revealing no other abnormalities. Both Peterson's defect and the small bowel mesenteric defect were completely closed with no evidence of internal hernia. The small bowel was inspected from the gastrojejunal anastomosis to the ileocecal valve, and from the ligament of Treitz to the jejunojejunal anastomosis, which revealed no abnormalities. The appendix and the gallbladder were absent given the patient's history of surgical resection. Her symptoms had significantly improved on postoperative day 1. Opioid analgesics were used on postoperative day 1 for pain control, and only acetaminophen was used for pain control starting postoperative day 2. She tolerated an oral diet well and demonstrated return of bowel function starting postoperative day 1; subsequently, she was discharged on postoperative day 2. She was followed up as an outpatient four weeks postoperatively and reported complete resolution of her symptoms. Informed consent was obtained for the publication of this case report.

Table 1. Patient's laboratory values on second Emergency Department visit.

Chemical profile	Value	Reference range
Leukocytes	**13.1 x10^9/L**	4.0 - 11.0 x10^9/L
Hemoglobin	149 g/L	130-180 g/L
Platelets	176 x10^9/L	150 - 400 x10^9/L
Sodium	137 mmol/L	135-145 mmol/L
Potassium	4.0 mmol/L	3.5-5.2 mmol/L
Chloride	107 mmol/L	95-110 mmol/L
CO2	20 mmol/L	20-29 mmol/L
Creatinine	55 µmol/L	60-110 µmol/L
eGFR	111 ml/min/1.73m^2	>60 ml/min/1.73m^2
Alkaline Phosphatase	**131 U/L**	38 - 126 U/L
Gamma Glutamyl Transferase	**102 U/L**	5-40 U/L
Aspartate Aminotransferase	**613 U/L**	18 - 54 U/L
Alanine Aminotransferase	**353 U/L**	0 - 49 U/L
Lipase	37	
Albumin	37	
Bilirubin, Total	**27 µmol/L**	<21 µmol /L
Bilirubin, Conjugated	**16 µmol/L**	≤ 19 µmol /L
Troponin	<3 ng/L	<35 ng/L

Discussion

Patients with a history of bariatric procedures presenting with abdominal pain pose a unique diagnostic challenge. There are well-recognized complications post-Roux-en-Y gastric bypass surgery that lead to abdominal pain, such as marginal ulcers, internal hernia, intra-abdominal adhesions, or biliary complications, for which well-established management remedies exist. However, when extensive investigations are inconclusive, both patients and the health system can endure prolonged hospital stays and consumption of resources for diagnostic purposes [2]. In such instances, diagnostic laparoscopy may detect pathologic findings in over half of all cases [3,4].

In this patient, both CT and MRCP detected hypoattenuation adjacent to the falciform ligament. This subtle finding should broaden the differential diagnosis of abdominal pain and lower the threshold for surgical exploration. Recognizing this abnormality, in conjunction with the clinical picture, can help guide timely surgical decision-making.

In laparoscopic RYGB, division of the greater omentum is a common practice aimed at reducing tension from the antecolic Roux limb on the gastrojejunal anastomosis [1]. However, routine division of the greater omentum has been scrutinized for its potential impact on postoperative complications. A study by Dallal and Bailey [1] reported a case of omental infarction after antecolic gastric bypass, suggesting that division of the omentum may contribute to such complications. A review by Alwatari et al. [5] demonstrated that almost all cases of omental infarction after RYGB required surgical exploration for diagnosis and management. This case, along with existing data, highlights diagnostic laparoscopy as an irreplaceable diagnostic and therapeutic tool in post-bariatric patients with undifferentiated abdominal pain.

Conclusion

In bariatric surgical patients, diagnostic laparoscopy offers a minimally invasive means of confirming intra-abdominal pathology that is not recognized on initial workup. It allows for the prompt identification and treatment of typical and atypical causes of abdominal pain. Overall, this case reinforces the crucial role of early surgical intervention in this patient population when the clinical picture is unclear. The decision to divide the greater omentum during RYGB should be carefully considered, weighing the potential benefits of reduced anastomotic tension against the risk of rare but serious complications like omental infarction.

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A case report of necrotizing fasciitis with a sole causative agent: *Actinotignum schaalii*

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Abstract

Actinotignum schaalii (*A. schaalii*) is a Gram-positive, anaerobic bacterium. While primarily associated with urinary tract infections in elderly and immunocompromised individuals, it has also been implicated in soft tissue infections such as necrotizing fasciitis. However, its role as a primary pathogen in necrotizing fasciitis outside the genitourinary region remains underreported. We present a case of necrotizing fasciitis of the axilla caused by *A. schaalii* in an elderly diabetic female. This case is unique in that it highlights the bacterium's role as the sole causative agent in a severe soft tissue infection, diverging from its typical polymicrobial involvement. This case emphasizes the pathogenic potential of *A. schaalii* in severe soft tissue infections and highlights the importance of advanced microbiological techniques for its accurate identification.

Keywords: necrotizing fasciitis, *Actinotignum schaalii*, soft tissue infections, anaerobic bacteria, infectious disease diagnostics, clinical case report, advanced diagnostic techniques, rare pathogens, MALDI-TOF, diabetes and infections

Introduction

Actinotignum schaali (*A. schaalii*) is a Gram-positive, anaerobic bacterium related to members of the genus *Actinomyces*. It is part of the microbiota primarily found in the genitourinary tract and on the skin. *A. schaalii* is associated with various human infections, particularly urinary tract infections in elderly and immunocompromised individuals. It has also been implicated in conditions such as bacteremia and soft tissue infections, and, less commonly, in osteomyelitis, and abscess formation [1]. Soft tissue infections caused by the *A. schaalii* bacteria are rare but are progressing rapidly [2-4]. The bacterium's involvement in severe polymicrobial infections, including necrotizing fasciitis, underscores its pathogenic potential. *A. schaalii* is frequently underreported, as it is slow-growing and difficult to phenotypically identify with typical microbiology laboratory techniques [5]. The slow growth and resemblance to the microbiota on the skin and mucous membranes contribute to its occasional misidentification [6].

We present a case of necrotizing fasciitis caused by *A. schaalii* in an elderly diabetic female patient. This case is significant because, although *A. schaalii* is most commonly associated with urinary tract infections (UTIs), it is rarely reported as a cause of skin infections [7]. While there are documented instances of Fournier's gangrene involving this pathogen in combination with other microorganisms [8], there is no evidence in the literature of *A. schaalii* acting as the sole causative agent of necrotizing fasciitis in different regions of the body. This makes our findings unprecedented.

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Informed Consent
The authors stated that the written consent was obtained from the patient presented with images in the study.

Conflict of Interest
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Case presentation

A 68-year-old female with a medical history of type 2 diabetes, obesity, and hypertension presented to the emergency department. Her diabetes was managed with gliclazide (60 mg daily), and hypertension was treated with ramipril 5 mg and indapamide 1.5 mg. She reported a two-day history of redness and painful swelling around her right armpit extending to the back and around the right breast.

On admission, her vital signs were as follows: respiratory rate, 15 breaths/min; SpO2, 95%; blood pressure, 139/77 mmHg; heart rate, 98 beats/min; and body temperature, 39°C. Physical examination revealed swelling of the right axillary fossa extending to the upper outer quadrant of the right breast, with visible pus-filled blisters and crepitus over the axilla extending to the scapula and the right thoracic wall. The remainder of the physical examination was unremarkable.

Initial laboratory diagnostic results revealed elevated levels of inflammatory markers, including white blood cell count and C-reactive protein, as detailed in Figure 1 and 2. Other laboratory values, such as a full blood count (FBC), urea and electrolytes (U&E), and clotting and arterial blood gas (ABG) tests, were initially within normal ranges.

Figure 1: Trend of white blood cell counts [normal: 4.50 - 11.00 x10^3], measured throughout the hospitalization, highlighting the correlation with the patient's treatment interventions and clinical progression.

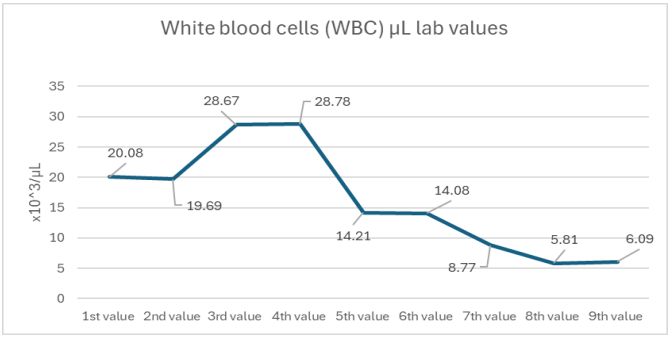
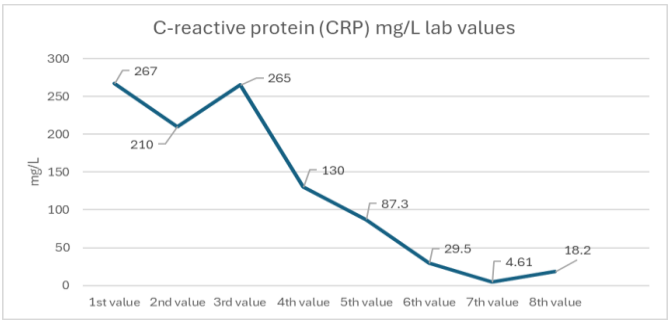


Figure 2: Trend of C-reactive protein (CRP) [normal: <5.00 mg/L] measured throughout the hospitalization, highlighting the correlation with the patient's treatment interventions and clinical progression.



A computerized tomography scan was performed and an extensive abscess-like collection with free gas in the area of the right armpit was seen, measuring approximately 9x12x10cm; extending from the axilla to the level of the 7-8th ribs, infiltrating to the anterior border of the pectoralis major muscle and posteriorly to the scapula. Visible gas penetration was observed spreading along the muscular fascia to the neck and the lower edge of the scapula, with further extension distally along the right upper extremity (Figure 3: panels A, B, C).

The patient was admitted to the Department of General Surgery. Empirical intravenous antibiotic therapy was immediately initiated with clindamycin 600 mg TDS and Cefotaxime 1 g BD, and an initial incision and drainage procedure was performed. This was followed by a series of extensive surgical debridements of infected subcutaneous tissue and fascia, with the concomitant application of negative pressure wound therapy (Figure 4: panels A, B, C). Surgical debridement was repeated until the wound was clear and covered with granulation tissue. Additionally, hyperbaric oxygen therapy was initiated on the sixth day of hospitalization.

The purulent fluid was immediately sent for microbiological culture. Initial microbiology results, obtained after three days, showed positive aerobic bacterial growth; however, the type of bacteria could not be determined. After 48 hours of incubation at 35°C on Columbia Agar with 5% sheep blood, small colony growth was observed. Following isolation, species identification was performed using mass spectrometry, which identified the pathogen as *A. schaalii*. Antimicrobial susceptibility testing of the strain was conducted on Mueller-Hinton agar enriched with horse blood and NAD. The diffusion method using gradient concentration strips (E-test) was employed to determine the minimum inhibitory concentration (MIC) values for selected antibiotics.

The final sensitivity results from the culture were available on the sixth postoperative day, showing *A. schaalii* as the sole pathogenic microorganism. The antibiotic sensitivity results presented minimum inhibitory concentrations of 0.0016 for both benzylpenicillin and ampicillin, 0.032 for Cefotaxime, 1.5 for ciprofloxacin, and 0.002 for trimethoprim/sulfamethoxazole. Due to the lack of breakpoint values available for this bacterium in EUCAST, the susceptibility could not be determined.

During hospitalization, the patient remained in good general condition. She was alert, oriented, and able to actively participate in her care. Vital signs remained stable throughout, and no significant complications were observed.

Written and signed informed consent was obtained from the patient for the publication of this case report. All identifying information has been anonymized to protect the patient's privacy.

Discussion

This is one of the few reported cases of *A. schaalii* causing necrotizing fasciitis. As stated by Könönen et al. [2], Actinomyces species have been detected at body sites where microbes are generally not found. Infections associated with *A. schaalii* typically involve the urinary tract and include cystitis, pyelonephritis, and urosepsis. However, other types of infections, especially those caused by *A. schaalii*, are increasingly being reported, including less frequent manifestations such as bacteremia, abscess formation, cellulitis, spondylodiscitis, bladder necrosis, epididymitis, and endocarditis [9].

A. schaalii belongs to the group of Gram-positive rods, many of which are considered harmless. This scenario has changed with the introduction of molecular testing, in particular, the use of 16S rRNA gene sequencing. This tool made it possible to identify bacteria more easily (tentatively to the species level). As a result, Gram-positive bacteria have being increasingly recognized as a cause of infection, including complicated skin and soft tissue infections (CSSI) [10]. Necrotizing infections and bacterial growth are rampant, and the species of bacteria can be rapidly identified [11].

Figure 3: A) Coronal view of Computed Tomography B) Sagittal view of Computed Tomography C) Axial view of Computed Tomography

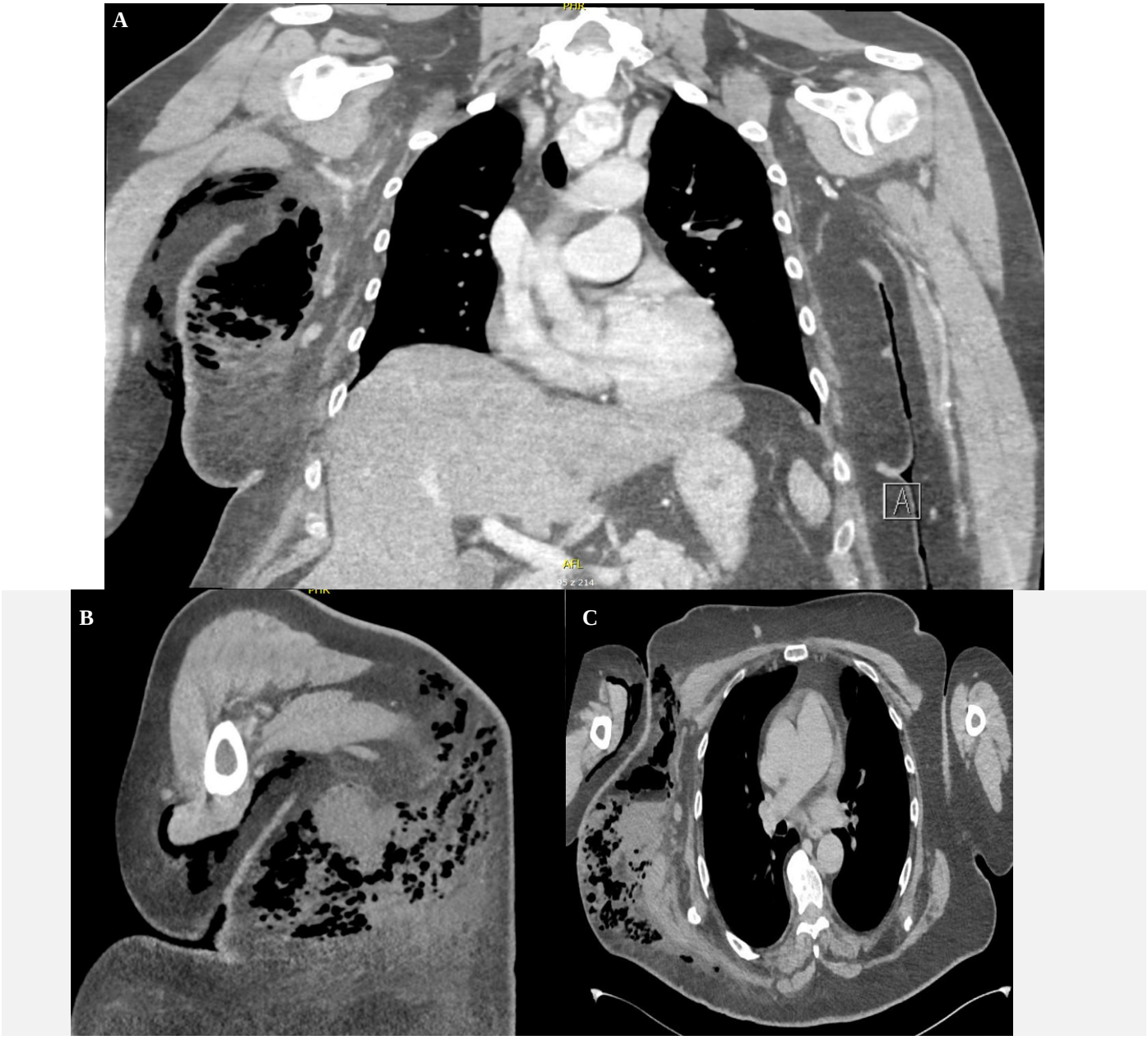
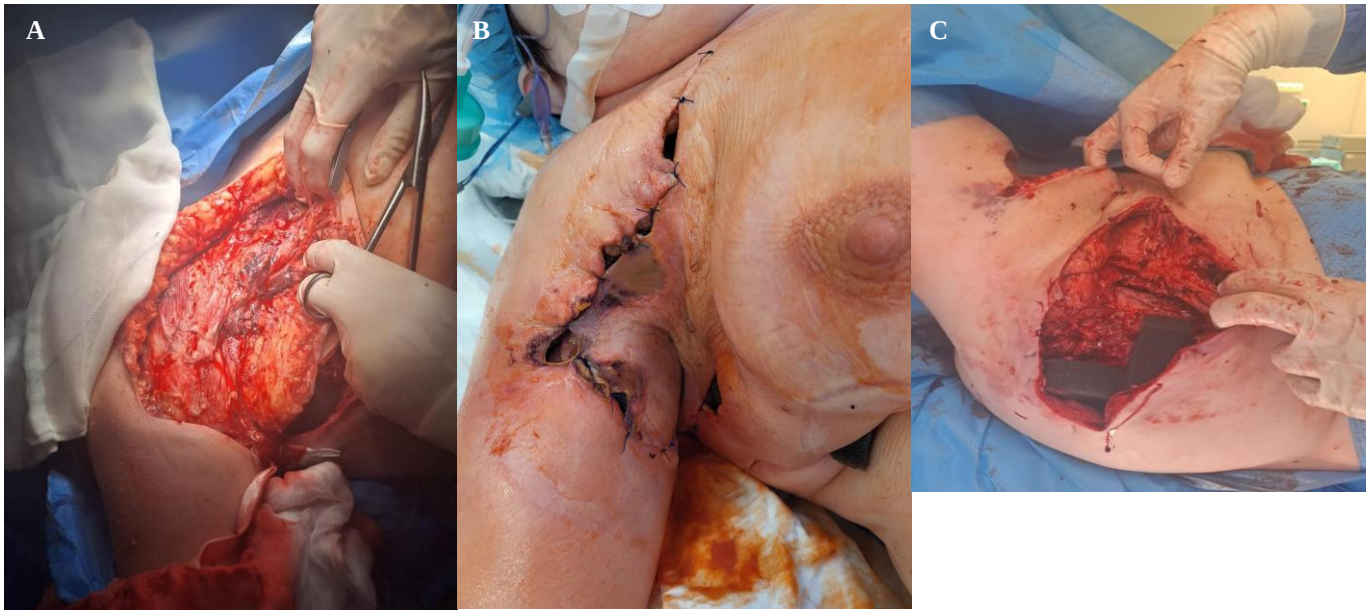


Figure 4: A) Clinical image depicting an intraoperative view of necrotizing fasciitis caused by *Actinotignum schaalii*, illustrating extensive soft tissue destruction. B) Clinical image of a surgical wound following debridement of necrotizing fasciitis in the right axillary region. C) Clinical images depicting an intraoperative view of necrotizing fasciitis caused by *A. schaalii*, illustrating extensive soft tissue destruction.



The clinical manifestations seen in our patient, which include an extensive abscess with gas formation, extensive inflammatory infiltration, and necrotizing fasciitis, are consistent with the aggressive nature of *A. schaalii*. One of the main challenges in managing infections caused by *A. schaalii* is the difficulty in detecting it in microbiological cultures. As mentioned above, identifying this pathogen typically requires advanced molecular techniques, such as 16S rRNA gene sequencing, real-time PCR, or spectrometry-based methods, which may not always be accessible [12]. The challenges in identifying *A. schaalii* underscore the importance of considering this organism in the differential diagnosis of soft tissue infections, particularly when the clinical presentation is severe and rapidly progressing, and when initial microbiological cultures do not yet yield a clear pathogen. For identification in our laboratory, mass spectrometry was used on the MALDI Biotyper Sirius System. Proteomic methods using mass spectrometry are based on analyzing the protein profile spectrum.

A. schaalii is considered a commensal bacterium of the urogenital system [13]. However, this species can cause UTI in elderly patients with urological disorders or with urinary catheters [14]. There are limited reports of *A. schaalii* being a part of polymicrobial pathogens in invasive infections, such as bacteremia or urosepsis, and skin infections [15]. The use of molecular genomic methods and proteomic diagnostics based on matrix-assisted laser desorption/ionization mass spectrometry (MALDI-TOF MS) has significantly improved detectability. The role of *A. schaalii* in infections is still underestimated due to the limited availability of diagnostic possibilities and tools.

Regarding other diseases caused by *A. schaalii*, identification using MALDI-TOF MS as the primary species identification method, combined with an increasing number of older persons with urinary tract morbidity, suggests that Actinotignum infections will likely be more frequently encountered [16]. In previous studies, it was shown that patients affected by UTIs are typically older males with underlying urinary tract conditions [17,18]. Due to the limited research evidence, it is challenging to confirm an age and gender correlation with *A. schaalii* infection in patients with complicated skin and soft tissue infections. However, elderly age, immune deficiency, and underlying diseases with symptoms may reflect the virulence of *A. schaalii* and the severity of the illness in elderly patients.

The management of *A. schaalii* infections is complex due to the lack of clear guidance on antibiotic sensitivity. In this case, the sensitivity testing did not provide a conclusive recommendation for the most effective antibiotic. *A. schaalii* based on results presented by Pedersen et al. [16] on antimicrobial susceptibility testing, β-lactams and vancomycin seem like feasible treatment options but resistance patterns can vary, and the presence of mixed infections with other bacteria can further complicate treatment decisions. Although there are no clear guidelines for the duration of antimicrobial therapy for *A. schaalii*-associated infections, it has been suggested that the duration should be at least two weeks [9].

In this patient, the prolongation of broad-spectrum antibiotics was necessary until the pathogen was identified and its antibiotic sensitivity profile could be assessed. In treatment, beta-lactam antibiotics are used and are effective. Commonly used antibiotics include penicillin, third-generation cephalosporins, carbapenems, and glycopeptides, with vancomycin being frequently employed.

The applicable interpretation guidelines, according to which drug susceptibility is assessed in Europe, including Poland, are the EUCAST guidelines. However, for the guidelines on the species *A. schaalii*, there are no specified interpretation ranges. Therefore, an antibiotic can be used in therapy based on positive literature data regarding its efficacy. The use of surgical debridement, combined with hyperbaric oxygen therapy, was a critical component of treatment to control the infection and promote healing in the affected tissues.

This case report highlights several important clinical implications. Primarily, it strengthens the need for awareness of *A. schaalii* as a potential pathogen in complicated skin and soft tissue infections, especially in patients with risk factors such as diabetes, immunosuppression, and obesity. It also exhibits the importance of early and aggressive intervention in cases of suspected necrotizing fasciitis, regardless of the initial pathogen in microbiological findings. Lastly, it points to the need for further research into the optimal management and identification of *A. schaalii* infections, including the development of more specific diagnostic tools and straightforward guidelines for antibiotic therapy.

Conclusion

The case of a 68-year-old female with necrotizing fasciitis caused by *A. schaalii* shows the complexity of diagnosing, identifying, managing, and treating infections caused by rare pathogens. It also underscores the pivotal role of advanced diagnostic techniques in detecting these pathogens and guiding to the appropriate and necessary treatment. Recently, such infections have become more frequently recognized due to improved diagnostic methods. Still, clinicians must remain observant in considering a broad range of potential pathogens, especially in patients presenting with atypical symptoms and significant underlying health conditions. Further research is needed to validate and confirm the clinical significance of these bacteria and establish the most effective treatment strategies.

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