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ACADEMIC JOURNAL OF HEALTH

ORIGINAL ARTICLE

A Seminar on Pregnancy Monitoring for Midwives and Evaluation of the Antenatal and Postnatal Care Services Provided in Northwest Syria

ABSTRACT

Background and Aims

Midwifery, one of the oldest professions in human history, is an independent healthcare discipline focused on maternal and child health. This study aimed to assess the existing healthcare services provided by a limited number of midwives in Northwest Syria. The assessment was conducted through a seminar designed to share knowledge on antenatal and postnatal care, using the questionnaire titled "Antenatal and Postnatal Monitoring Services Provided in Northwest Syria", which was developed to evaluate the scope and quality of maternal health services delivered by midwives.

Methods

A total of 80 midwives who met the inclusion criteria and agreed to participate were included in the study. Data were collected using a two-part questionnaire entitled "Antenatal and Postnatal Monitoring Services Provided in Northwest Syria."

Results

The mean age of the participants was 33.80 ± 9.15 years. Among the participants, 66.3% (n = 53) were employed in hospitals, and 43.8% (n = 35) had more than 10 years of professional experience.

Conclusion

Improving the quality of healthcare services in the region by enhancing midwives' knowledge and skills, providing appropriate working conditions, and addressing social determinants of health may lead to significant improvements in both maternal and child health outcomes. Such interventions may also help mitigate the adverse effects of war on physical and psychological well-being.

Keywords: Antenatal care, Midwife, Postnatal care, Pregnancy, Syria

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Introduction

Midwifery, one of the oldest professions in human history, is a specialized, professional, and independent healthcare discipline focused on maternal and child health. A midwife is a certified healthcare provider who serves women and newborns simultaneously, assuming critical responsibilities to ensure their well-being (1,2). Midwives play a vital role in maintaining and promoting health by providing education and counseling not only to women and children but also to families and communities, thereby contributing to the protection, promotion, and advancement of public health. According to the World Health Organization (WHO), a midwife is a trained and certified professional responsible for providing care and counseling during pregnancy, childbirth, and the postpartum period, as well as independently managing normal deliveries and caring for newborns (1).

In well-resourced healthcare systems, adequately planned and effectively implemented midwifery practices can have a substantial positive impact on maternal and neonatal health outcomes, potentially preventing approximately two-thirds (66%) of maternal deaths. Investments in midwifery services are therefore considered

essential for building healthier and more prosperous societies (2).

It is well documented that wars and armed conflicts adversely affect public health, particularly among women and children, highlighting the importance of social stability as a key determinant of health. The conflict in Syria represents a striking example. Prior to the war, Syria had achieved notable public health successes, including low infant mortality rates and high vaccination coverage. However, these indicators deteriorated rapidly following the onset of conflict. The severity of the impact on child health is illustrated by the increase in infant mortality rates from 14 per 1,000 live births in Syria in 2010 to 290 per 1,000 live births among Syrian refugees in Lebanon. In the post-conflict period, Syria has faced profound setbacks in maternal and child health, resulting in major public health challenges (3).

This study aimed to assess the healthcare services provided by a limited number of midwives in Northwest Syria by evaluating a seminar designed to share knowledge on antenatal and postnatal care. The findings are expected to inform future midwifery training programs and contribute to improving health outcomes in communities affected by war.

Materials and Methods

Study Design

This study was a cross-sectional study conducted through face-to-face interviews with midwives working in Northwest Syria. The aim of the study was to assess prenatal, antenatal, and postpartum health surveillance services and to provide recommendations for improving midwifery practices in the region. A total of 267 midwives were employed in hospitals and health centers in Northern Syria. Due to security concerns, midwives working in inaccessible areas could not be included; therefore, the target sample size was set at 123 midwives.

Ethical approval for the study was obtained from the Noninterventional Research Ethics Committee of Hatay Mustafa Kemal University (Date: 06.05.2021, Decision No: 22). In addition, necessary permissions were obtained from local health authorities and relevant organizations. The study was conducted in accordance with the principles of the Declaration of Helsinki issued by the World Medical Association.

Study Setting

The study was conducted among midwives working in various health centers and hospitals in Northwest Syria. In this region, healthcare services have been largely restructured following the war, and healthcare professionals provide services to a large patient population under limited-resource conditions. The study focused on midwifery practices, particularly those related to prenatal and postpartum surveillance services.

Participant Selection

The study included midwives working in Northwest Syria who were actively engaged in providing prenatal and postpartum surveillance services. Inclusion criteria were being aged 18 years or older, actively practicing midwifery in Northern Syria, and providing voluntary informed consent to participate. A total of 123 midwives met the inclusion criteria. Forty-three healthcare personnel were excluded because they declined participation, were under the age of 18, or did not provide direct midwifery services. Ultimately, 80 midwives who met the inclusion criteria and agreed to participate were included in the study.

Data Collection

The questionnaire titled “Antenatal and Postnatal Monitoring Services Provided in Northwest Syria” was developed in Turkish following a comprehensive review of the literature and subsequently translated into Arabic by sworn translators. The clarity and appropriateness of the questions were evaluated by Syrian specialist physicians experienced in regional healthcare practices. Following a pilot study conducted with 20 participants, questions that were misunderstood were removed, and the questionnaire was finalized.

The questionnaire consisted of two sections. The first section addressed sociodemographic characteristics, including age, education level, marital status, and working conditions. The second section assessed knowledge, attitudes, and practices related to prenatal care, pregnancy, and postpartum surveillance services.

Participants were informed about the purpose of the study, and guidance was provided to ensure complete and accurate responses. Collected data were recorded in a digital format suitable for statistical analysis and subsequently analyzed.

Statistical Analysis

Statistical analyses were performed using JASP (version 0.19.0) and R (version 4.4.1). In R, analyses were conducted using the stats and rstatix packages. Descriptive statistics were reported as mean ± standard deviation, median (minimum–maximum; interquartile range [IQR]), and frequency (n, %). Normality was assessed using the Shapiro–Wilk and Kolmogorov–Smirnov tests.

Comparisons among more than two groups were performed using the Kruskal–Wallis test. When significant differences were detected, pairwise post-hoc comparisons were conducted using Dunn’s test with Benjamini–Hochberg false discovery rate (FDR) adjustment. Comparisons between two groups were performed using the Mann–Whitney U test. Effect sizes were calculated as $r = Z/\sqrt{n}$ for Mann–Whitney U tests and eta-squared $(\eta^2) = (H - k + 1)/(n - k)$ for Kruskal–Wallis tests. Categorical variables were analyzed using Pearson’s chi-square test or the Fisher–Freeman–Halton exact test, as appropriate. Proportions were presented with 95% confidence intervals calculated using the exact binomial (Clopper–Pearson) method. All p-values were two-sided and reported to three decimal places ($\alpha = 0.050$).

Results

A total of 80 midwives participated in the study. Of these, 66.3% (n = 53) were employed in hospitals, and 43.8% (n = 35) had more than 10 years of professional experience. The mean age of the participants was 33.80 ± 9.15 years. Regarding educational level, 35.0% (n = 28) held an associate degree, 27.5% (n = 22) held a bachelor's degree, and 23.8% (n = 19) had completed high school education. In addition, 66.2% (n = 53) were married, and 60.0% (n = 48) had children.

Regarding place of residence, 42.3% lived in urban areas and 33.3% (n = 26) in rural villages. Most participants (95.0%, n = 76) lived in private homes, while 5.0% (n = 4) resided in camps. The distribution of midwives' practices and perspectives related to pregnancy, childbirth, and postpartum care is presented in Table 1.

The median monthly income was 2,550 TRY (range: 500–12,750). A statistically significant increase in income was observed with higher educational attainment. Midwives with a high school diploma reported a median income of 1,000 TRY (800–3,700), whereas those with postgraduate education reported a median income of 2,975 TRY (900–7,650) (p = 0.026). Home visit practices differed significantly by education level, with 72.7% of bachelor's degree holders conducting home visits compared with 18.2% of those with postgraduate education (p = 0.003). This finding may suggest that bachelor-level midwives are more involved in fieldwork, whereas those with postgraduate qualifications may assume more advisory or administrative roles. A significant difference was also observed in ultrasound usage (p = 0.005), with usage rates highest among midwives with postgraduate education (Table 2).

A statistically significant association was found between place of residence and the ability to contact pregnant women who missed follow-up appointments (p = 0.015). Success rates were 33.3% in urban areas, 35.3% in districts, 69.2% in villages, and 100% in other settings (Table 3).

Differences in monthly income and working hours according to education level and professional experience are shown in Table 4. The Kruskal–Wallis test revealed a significant difference among education groups (p = 0.026). Pairwise comparisons indicated significant differences between Group 1 and Groups 2, 3, and 4. A significant difference was also observed between professional experience groups (p = 0.006), particularly between midwives with 1–5 years and those with more than 10 years of experience.

Discussion

Midwifery has evolved into a professional healthcare discipline grounded in scientific knowledge, ethical principles, and evidence-based practice. Midwives provide monitoring, care, counseling, and education throughout pregnancy, childbirth, the postpartum period, and the neonatal stage, thereby contributing significantly to the health of women, families, and communities (2).

Wars and conflicts pose severe threats to public health, particularly for women and children. In Syria, prolonged conflict has led to increased preventable disabilities, communicable diseases, and mortality (3). Despite limited resources and challenging conditions, midwives demonstrated strong professional commitment, although the lack of equipment and training negatively affected the quality of care. These findings underscore the urgent need to improve working environments.

Regular prenatal care is essential for reducing maternal and neonatal morbidity and mortality (4,5). In the present study, although attendance rates were relatively high, home visits remained underutilized. Expanding home visit services may improve access to prenatal care, particularly for women facing barriers to healthcare facilities.

Refugee women often experience limited access to reproductive health information and services due to sociocultural and economic constraints (5,10). In this study, malnutrition was the most common health problem among pregnant women, followed by hypertension and gestational diabetes. These conditions are largely preventable through education and early intervention, highlighting the critical role of midwives in community-based healthcare.

Conclusion

In Northwest Syria, prenatal and postnatal care services provided by midwives have been significantly disrupted by ongoing conflict. Although midwives remain committed to providing care, environmental limitations, financial constraints, and insufficient community awareness hinder effective service delivery.

Strengthening midwives' knowledge and skills through in-service training, improving working conditions, and addressing social determinants of health may enhance the quality of maternal and child healthcare services. Such efforts have the potential to mitigate the long-term physical and psychological effects of war on vulnerable populations.

Declarations

The authors declare that there are no conflicts of interest, financial support, or commercial relationships that could be perceived as influencing the research presented in this manuscript. Ethical approval was obtained from the Noninterventional Research Ethics Committee of Hatay Mustafa Kemal University (Date: 06.05.2021, Decision No: 22).

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Tables

Table 1. Distribution of Midwives' Practices in Pregnancy, Delivery, and Postpartum Care in Northwestern Syria

	N (%)
Years of Professional Experience	
1-5 years	27 (33.8)
5-10 years	18 (22.5)
10 years and above	35 (43.8)
Which institution do you currently work for?	
Hospital	53 (66.3)
Hospital + Health Center	4 (5.0)
Health Center	22 (27.5)
Health Center + Private Clinic	1 (1.3)
Average monthly working hour? *Mean SD,Median(Min-Max)*	245.66 78.99 240 (90-520)
How many times do pregnant women attend follow-up visits during 9 months?	
1-2	2 (2.5)
2-4	11 (13.8)
4-6	34 (42.5)
6-8	33 (41.3)
If you work at a health center, do you conduct home visits?	
Yes	44 (55.0)
No	36 (45.0)
Can pregnant women obtain prescribed medications free of charge?	
They can afford them	13 (16.3)
They cannot afford them when the medication is out of stock	42 (52.5)
They can never afford them	16 (20.0)
Missing	9 (11.2)
Do you request blood or urine tests from pregnant women?	
Yes	71 (88.8)
No	3 (3.8)
Missing	6 (7.5)
If your answer is "Yes", please indicate the tests you request:	
Hemogram	46 (16.6)
ABO + Rh typing	58 (20.9)
Hepatitis	46 (16.6)
Toxoplazmosis	24 (8.7)
Rubella	4 (1.4)
CMV Ig testing	9 (3.2)
TSH	4 (1.4)
Urine test	57 (20.6)
Other	4 (1.4)
What are the most common health problems you encounter in pregnant women? (You can select multiple options)	
Hypertension	63 (17.0)
Gestational Diabetes	47 (12.7)
Preeclampsia	39 (10.5)
Heart diseases	13 (3.5)
Nutritional deficiency	67 (18.1)
Pregnancy under 18 years of age	40 (10.8)
Multiple pregnancy	32 (8.65)
Vaginal infections	25 (6.76)
Urinary tract infections	43 (11.6)
Other	1 (0.3)
Do you refer pregnant women with detected risks to the hospital?	
Yes	74 (92.5)
No	2 (2.5)
missing	4 (5.0)
Do you use ultrasound?	

Yes	40 (50.0)
No	40 (50.0)
Do you know how to apply and interpret NST (Non-Stress Test) for pregnant women?	
Yes	43 (53.8)
No	37 (46.2)
Do you assist with home births?	
Yes	22 (27.5)
No	58 (72.5)
In your opinion, do women prefer to give birth at home or in a hospital more?	
At home	19 (23.8)
İn a hospital	61 (76.3)
What is the most common issue you encounter with births you attend?	
Preterm birth	49 (26.1)
Breech presentation	35 (18.6)
Shoulder dystocia	21 (11.2)
Vaginal infection	17 (9.0)
Macrosomia (large baby)	25 (13.3)
Prolonged labor	34 (18.1)
Other	7 (3.7)
What problems do you encounter during the postpartum period?	
Atony	34 (18.1)
Infection	29 (15.4)
Other	16 (8.5)
Is postpartum follow-up provided to mothers?	
Yes	60 (75.0)
No	11 (13.8)
Missing	9 (11.3)
If your answer is "Yes", how many times is the follow-up conducted?	
1	4 (12.1)
2	16 (48.5)
3	7 (21.2)
4	6 (18.2)
Do you provide breastfeeding and counseling services to postpartum women?	
Yes	70 (87.5)
No	6 (7.5)
Missing	4 (5.0)
Do you have patients who approach you for postpartum depression?	
Yes	40 (50.0)
No	33 (41.3)
Missing	7 (8.8)
What is your approach when a patient approaches you with postpartum depression?	
Referral to a social support specialist	48 (60.8)
Referral to a psychological counselor	18 (22.8)
Referral to a psychiatrist	10 (12.7)
Other	3 (3.8)
What are the most common health problems you encounter in newborns?	
Low birth weight	50 (25.6)
Congenital anomalies	17 (8.7)
Respiratory problems	52 (26.7)
Feeding problems	19 (9.7)
Jaundice	53 (27.2)
Other	4 (2.0)
Do you like your profession?	
Yes	73 (91.3)
No	1 (1.3)
Missing	6 (7.5)
What do you need to perform your midwifery profession better?	
Ultrasound device	35 (34.3)
Surgical instruments for family planning	24 (23.5)
In-service training	38 (37.2)
Other	5 (4.9)

What topics would you like to receive in-service training on?	
Pregnancy examination and follow-up	48 (14.6)
High-risk pregnancies	42 (12.8)
Ultrasound/NSTusage	55 (16.7)
Childbirth/ High-risk childbirth	49 (14.9)
Episiotomy	11 (3.3)
Postpartum period	20 (6.1)
Neonatal care	37 (11.3)
Education for women/Family planning methods	63 (19.2)
Other	3 (0.9)

Table 2. Comparison of Midwives' Practices by Educational Level

	Total	**High School**	**Associate Degree**	**Undergraduate Degree**	**Graduate Degree**	**p**
If you work at a health center, do you conduct home visits? n(%)						
Yes	44(55.0)	14(73.7)	12(42.9)	16(72.7)	2(18.2)	**0.003**[#]
No	36(45.0)	5(26.3)	16(57.1)	6(27.3)	9(81.8)	
Do you use ultrasound? n(%)						
Yes	40(50.0%)	8(42.1)	16(57.1)	6(27.3)	10(90.9)	**0.005**[*]
No	40(50.0%)	11(57.9)	12(42.9)	16(72.7)	1(9.1)	
Do you know how to apply and interpret NST (Non-Stress Test) for pregnant women? n(%)						
Yes	43(53.8)	12(63.2)	13(46.4)	14(63.6)	4(36.4)	0.323[*]
No	37(46.2)	7(36.8)	15(53.6)	8(36.4)	7(63.6)	
Do you assist with home births?n(%)						
Yes	22(27.5)	4(21.1)	7(25.0)	6(27.3)	5(45.5)	0.565[#]
No	58(72.5)	15(78.9)	21(75.0)	16(72.7)	6(54.5)	
Do you provide breastfeeding and counseling services to postpartum women? n(%)						
Yes	70(87.5)	15(78.9)	24(85.7)	20(90.9)	11(100.0)	0.835[#]
No	6(7.5)	2(10.5)	3(10.7)	1(4.5)	0(0.0)	
Do you like your profession? n(%)						
Yes	73(91.3)	18(100.0)	26(100.0)	18(94.7)	11(100.0)	0.651[#]
No	1(1.3)	0(0.0)	0(0.0)	1(5.3)	0(0.0)	

[&]: Kruskal Wallis, [#]: Fisher Freeman Halton Exact test, [*]: Chi-Square test

Table 3. Access to Health Services and Practices by Place of Residence

	Total	City	District	Village	Other	p
	n=80	n=33(42.3)	n=18(23.1)	n=26(33.3)	n=1(1.3)	
When pregnant women do not attend follow-up visits, do you have a chance to contact them? n(%)						
Yes	36(46.8)	11(33.3)	6(35.3)	18(69.2)	1(100.0)	0.015[#]
No	41(53.2)	22(66.7)	11(64.7)	8(30.8)	0(0.0)	
If you work at a health center, do you conduct home visits? n(%)						
Yes	44(55.0)	19(57.6)	9(50.0)	15(57.7)	0(0.0)	0.794[#]
No	36(45.0)	14(42.4)	9(50.0)	11(42.3)	1(100.0)	
Do you use ultrasound? n(%)						
Yes	40(50.0)	20(60.6)	5(27.8)	13(50.0)	1(100.0)	0.082[#]
No	40(50.0)	13(39.4)	13(72.2)	13(50.0)	0(0.0)	
Do you know how to apply and interpret NST (Non-Stress Test) for pregnant women? n(%)						
Yes	43(53.8)	19(57.6)	7(38.9)	16(61.5)	0(0.0)	0.269[#]
No	37(46.2)	14(42.4)	11(61.1)	10(38.5)	1(100.0)	
Do you assist with home births?n(%)						
Yes	22(27.5)	10(30.3)	7(38.9)	4(15.4)	0(0.0)	0.265[#]
No	58(72.5)	23(69.7)	11(61.1)	22(84.6)	1(100.0)	
In your opinion, do women prefer to give birth at home or in a hospital more? n(%)						
Home	19(23.8)	6(18.2)	3(16.7)	9(34.6)	0(0.0)	0.419[#]
Hospital	61(76.3)	27(81.8)	15(83.3)	17(65.4)	1(100.0)	
Is postpartum follow-up provided to mothers? n(%)						
Yes	60(75.0)	22(66.7)	17(94.4)	18(69.2)	1(100.0)	0.256[#]
No	11(13.8)	7(21.2)	1(5.6)	3(11.5)	0(0.0)	
Do you provide breastfeeding and counseling services to postpartum women? n(%)						
Yes	70(87.5)	28(84.8)	16(88.9)	24(92.3)	1(100.0)	0.583[#]

No	6(7.5)	2(6.1)	2(11.1)	2(7.7)	0(0.0)	
Do you like your profession? n(%)						
Yes	73(91.3)	29(100.0)	18(100.0)	23(95.8)	1(100.0)	0.594#
No	1(1.3)	0(0.0)	0(0.0)	1(4.2)	0(0.0)	

#: Fisher-Freeman Halton Exact test, &: Kruskal Wallis Test

Table 4. Comparison of monthly income and working hours by educational status and professional experience

Variables	Average Monthly Income Median(Min-Max)	Working Hours Median(Min-Max)
Education Level		
High School (1)	1000(800-3700)	216(120-312)
Associate Degree (2)	2150(500-11050)	240(144-424)
Bachelor's (3)	2550(850-12750)	240(90-520)
Postgraduate (4)	2975(900-7650)	240(180-312)
p&	***0.026***	*0.262*
p1-2	***0.039***	
p1-3	***0.021***	
p1-4	***0.039***	
p2-3	*0.156*	
p2-4	*0.575*	
p3-4	*0.132*	
Professional Experience		
1–5 years	900(500-4250)	240(144-450)
5–10 years	1850(900-12750)	228(150-315)
10+ years	2975(850-11050)	240(90-520)
p&	*0.006*	*0.613*
p1-5-5-10	*0.171*	
p1-5-10+	***0.006***	
p5-10,10+	*0.140*	

&: Kruskal–Wallis test; other p-values are from pairwise comparisons conducted using the Mann–Whitney U test, adjusted with the Benjamini–Hochberg correction.(**p_{1-2}**: Comparison between High School and Associate Degree groups, **p_{1-3}**: Comparison between High School and Bachelor's Degree groups, **p_{1-4}**: Comparison between High School and Postgraduate groups, **p_{2-3}**: Comparison between Associate Degree and Bachelor's Degree groups, **p_{2-4}**: Comparison between Associate Degree and Postgraduate groups, **p_{3-4}**: Comparison between Bachelor's Degree and Postgraduate groups)

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ACADEMIC JOURNAL OF HEALTH

ORIGINAL ARTICLE

Antibiotic Susceptibilities of Escherichia coli and Klebsiella pneumoniae Isolates from Clinical Samples: 3-Year Analysis

ABSTRACT

Objectives

This study presents antibiotic susceptibility data for Escherichia coli (E. coli) and Klebsiella pneumoniae (K. pneumoniae) isolates recovered in our hospital between January 1, 2020, and December 31, 2022.

Methods

Over the 3-year period, we analyzed annual antibiograms and extended-spectrum β-lactamase (ESBL) positivity rates of E. coli and K. pneumoniae isolates recovered from urine and non-urine clinical specimens submitted to the clinical microbiology laboratory. Only isolates identified as causative agents of infection in adult patients were included. Data were stratified by specimen type into urinary and non-urinary groups; non-urinary specimens comprised blood, respiratory, and cerebrospinal fluid (CSF) samples. Antimicrobial susceptibility testing was performed using the disk diffusion method and the VITEK®2 Compact automated system (bioMérieux, France). ESBL production was assessed using the double-disk synergy test and the automated system. Antibiogram quality control was routinely performed monthly.

Results

A total of 4,129 E. coli and 1,385 K. pneumoniae isolates were included. Overall ESBL positivity was 21.0% for E. coli and 33.2% for Klebsiella spp. Over the study period, E. coli isolates showed susceptibility rates exceeding 80% for carbapenems, aminoglycosides, ceftriaxone, and fosfomycin.

Conclusion

Determining susceptibility profiles and ESBL positivity rates for commonly isolated pathogens such as E. coli and K. pneumoniae is critical. Healthcare institutions should perform these analyses regularly in accordance with national and international guidelines and share results with relevant stakeholders. Such efforts support local and national antimicrobial stewardship programs and guide empirical therapy strategies.

Keywords: Escherichia coli; ESBL; Klebsiella pneumoniae; antimicrobial susceptibility

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Introduction

Year-to-year and regional variation in antimicrobial resistance is clinically important, particularly for selecting empirical therapy in hospitalized patients and reducing morbidity and mortality (1). Antimicrobial resistance (AMR) is an escalating global health threat that requires urgent action through international collaboration (2). The World Health Organization (WHO) has projected that, without effective preventive measures, AMR could contribute to up to 10 million deaths annually by 2050 (3).

Institution-level surveillance of antimicrobial susceptibility patterns is essential for guiding empirical therapy (4–6). In this context, monitoring resistance trends among WHO-designated critical- and high-priority pathogens—often discussed in relation to ESKAPE organisms (7,8)—is particularly important.

Among Gram-negative bacteria, extended-spectrum β-lactamase (ESBL) production is a major mechanism of β-lactam resistance (9,10). Members of the Enterobacterales family, especially E. coli and K. pneumoniae, may hydrolyze penicillins and third-

generation cephalosporins via ESBL production, making detection and reporting of ESBLs crucial in both clinical care and microbiology laboratories (11). ESBL genes are frequently associated with co-resistance to other antimicrobial classes, further complicating therapy (11,12). Consequently, rising resistance contributes to increased morbidity and mortality (13).

Regular evaluation of institutional antibiogram data helps prevent the use of ineffective agents and reduces unnecessary use of broad-spectrum antibiotics when isolate-specific results are not yet available. Such analyses support appropriate empirical regimens and inform stewardship policies (4,14). Therefore, we aimed to analyze antibiotic susceptibility and ESBL positivity rates of E. coli and K. pneumoniae isolates recovered between January 2020 and December 2022.

Materials and Methods

Clinical isolates of E. coli and K. pneumoniae were obtained from cultures submitted to the clinical microbiology laboratory from adult inpatients and outpatients at Sincan Training and Research Hospital. Isolates were considered causative agents based on leukocyte presence, pure growth, and criteria defined by national and international guidelines. Antimicrobial susceptibility test results for isolates collected between January 1, 2020, and December 31, 2022, were retrospectively analyzed.

Clinical specimens were inoculated onto 5% sheep blood agar and eosin methylene blue (EMB) agar using sterile loops and incubated aerobically at 35–37°C. After overnight incubation, growth was evaluated. For normally sterile specimens (e.g., CSF and pleural fluid), if no growth was observed, incubation was extended for an additional 48 hours before final reporting.

Bacterial identification and antimicrobial susceptibility testing were performed using conventional methods and the VITEK®2 Compact automated system (bioMérieux, France). Susceptibility results were interpreted according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. Data were stratified by specimen type as urine versus non-urine (blood, respiratory samples, and CSF), according to the number of isolates available for each category.

To minimize redundancy, duplicate isolates from the same patient were excluded and only the first isolate was included. Due to low isolate counts (<30), organisms recovered from pleural fluid, pericardial fluid, and other uncommon specimen types were excluded.

In our laboratory, susceptibility testing for urinary E. coli isolates is routinely performed using disk diffusion in accordance with EUCAST guidelines (version 13.0, 2023). Disks (Bioanalyse®, Türkiye) included amikacin (AN, 30 µg), gentamicin (GN, 10 µg), ampicillin (AM, 10 µg), amoxicillin/clavulanic acid (AMC, 20/10 µg), ceftriaxone (CRO, 30 µg), cefepime (FEP, 30 µg), trimethoprim/sulfamethoxazole (SXT, 1.25/23.75 µg), piperacillin/tazobactam (TZP, 30/6 µg), fosfomycin (FOS, 200 µg; only for uncomplicated E. coli urinary tract infection), meropenem (MEM, 10 µg), and ciprofloxacin (CIP, 5 µg).

For isolates from non-ICU patients, disk diffusion was used, whereas isolates from ICU patients were tested using the VITEK®2 system.

ESBL production was assessed using the double-disk synergy test and the VITEK®2 system, as previously described by Akpaka et al. (10). Quality control of susceptibility testing was performed monthly.

Ethical approval was obtained from the Ankara Bilkent City Hospital Clinical Research Ethics Committee (Decision No: E1-23-4360).

Statistical Analysis

ESBL positivity and antibiotic susceptibility rates were calculated descriptively.

Results

During the 3-year period, 4,129 E. coli and 1,385 K. pneumoniae isolates were included. Among E. coli isolates, 2,448 (59.3%) were obtained from outpatients and 1,681 (40.7%) from hospitalized patients. For K. pneumoniae, 432 (31.2%) isolates were from outpatients and 953 (68.8%) from hospitalized patients.

In 2020, 1,192 E. coli and 424 K. pneumoniae isolates were recovered; 914 (76.7%) and 313 (73.8%) of these, respectively, originated from urine specimens. (If “A total of 914 urine isolates were analysed over the three-year period” is correct, this sentence should be clarified because 914 is already the 2020 urine count.)

E. coli accounted for 57% of isolates in 2020, 58% in 2021, and 61% in 2022. For K. pneumoniae, the corresponding proportions were 19% (n = 313), 20% (n = 299), and 17% (n = 419), respectively. The overall median age was 45 years. Of 5,514 patients, 3,606 (65.4%) were female and 1,908 (34.6%) were male. Median age was 39 years (range: 18–99) in females and 56 years (range: 18–90) in males.

ESBL positivity rates for E. coli and K. pneumoniae were 20.3% (242/1,192) and 35.2% (150/425) in 2020, 21.1% (228/1,076) and 34.9% (148/424) in 2021, and 21.4% (401/1,866) and 30.4% (163/536) in 2022, respectively.

For E. coli, susceptibility rates exceeding 90% were observed for meropenem, piperacillin/tazobactam, ceftriaxone, and fosfomycin. For K. pneumoniae, the highest susceptibility was observed for meropenem (>90%). Annual isolate counts and susceptibility distributions are presented in Tables 1–3.

Discussion

Analysis and reporting of institutional susceptibility data are central to antimicrobial stewardship. Because identification and susceptibility testing may take time, institution-specific antibiogram data can support appropriate empirical therapy selection (14–16). Regional resistance patterns vary, and institutional data complement clinical guidelines in guiding

empirical choices (17).

Previous studies have reported that susceptibility rates for K. pneumoniae are often lower in non-urine specimens than in urine specimens, consistent with our findings. In our dataset, E. coli showed the highest susceptibility (>90%) to amikacin, ceftriaxone, piperacillin/tazobactam, and meropenem, while meropenem showed the highest susceptibility among K. pneumoniae isolates (>90%).

According to the 2023 CAESAR report (based on 2021 data), resistance rates for E. coli and K. pneumoniae vary substantially across regions, with high resistance to third-generation cephalosporins and fluoroquinolones reported in many settings (18). Urinary tract infections remain among the most common adult infections, with E. coli the leading pathogen and K. pneumoniae also frequently isolated (19). Multiple studies have similarly highlighted carbapenems and amikacin among the most active agents, while resistance to ciprofloxacin, trimethoprim/sulfamethoxazole, and ceftriaxone may be substantial depending on region and setting (20).

Comparing our findings with earlier institutional data suggests a modest increase in ESBL positivity over time. In the present study, ESBL positivity was 21.0% (871/4,129) for E. coli and 33.2% (461/1,385) for Klebsiella spp., indicating a continuing upward trend and reinforcing the need for coordinated stewardship efforts between clinical and microbiology teams.

This study included only adult patients and demonstrated a slight increase in resistance rates over time. The larger number of processed specimens in 2022 may reflect increased routine hospital attendance following the containment of the COVID-19 pandemic. Continued emphasis on infection prevention measures is warranted.

Conclusion

The increasing prevalence of antimicrobial resistance is concerning. Carbapenems remain among the most reliable treatment options in settings with high ESBL rates. Routine surveillance of susceptibility and ESBL positivity for common pathogens such as E. coli and K. pneumoniae is essential for guiding empirical therapy and supporting antimicrobial stewardship. Institutions should conduct these analyses regularly in accordance with national and international guidelines and disseminate findings to relevant stakeholders to inform local and national stewardship initiatives and empirical treatment strategies.

Author Contributions

All authors contributed to conception and study design, data acquisition/analysis, and manuscript drafting and revision.

Declarations

Ethics Committee Approval: Approved by the Ankara Bilkent City Hospital Clinical Research Ethics Committee (Decision No: E1-23-4360).

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This can be attributed to the increase in routine hospital visits following the containment of the COVD-19 pandemic. In addition, it is imperative that infection prevention measures are taken.

Table 1. Antibiotic Susceptibility Rates of *E. coli* and *K. pneumoniae* Isolates in 2020 (%)

Antibiotic Disk	*E. coli* Urine (%)	*E. coli* Non-urine (%)	Antibiotic Disk	*K. pneumoniae* Urine (%)	*K. pneumoniae* Non-urine (%)
AN	98	94	AN	64	53
GN	81	43	GN	75	58
AM	24	13	AM	4	3
AMC	55	35	AMC	36	13
CRO	96	91	CRO	74	65
FEP	83	54	FEP	69	62
SXT	59	26	SXT	63	37
TZP	90	90	TZP	82	72
FOS*	95	NT	FOS	NT	NT
MEM	99	96	MEM	92	86
CIP	63	52	CIP	75	70
Total	n:914	n:278	Total	n:313	n:112

***Non-urine**: CSF (Cerebrospinal Fluid), Blood, DTA (Deep Tracheal Aspirate), Sputum, Wound Culture Samples *: Only for E. coli NT: Not tested*

AN (Amikacin), GN (Gentamicin), AM (Ampicillin), AMC (Amoxicillin/Clavulanic Acid), CRO (Ceftriaxone), FEP (Cefepime), SXT (Trimethoprim/Sulfamethoxazole), TZP (Piperacillin/Tazobactam), FOS (Fosfomycin), MEM (Meropenem), CIP (Ciprofloxacin)

Table 2. Antibiotic Susceptibility Rates of *E. coli* and *K. pneumoniae* Isolates in 2021 (%)

Antibiotic Disk	*E. coli* Urine (%)	*E. coli* Non-urine (%)	Antibiotic Disk	*K. pneumoniae* Urine (%)	*K. pneumoniae* Non-urine (%)
AN	97	93	AN	65	55
GN	85	53	GN	77	63
AM	30	16	AM	4	3
AMC	57	34	AMC	33	12
CRO	92	88	CRO	62	50
FEP	81	54	FEP	70	61
SXT	52	26	SXT	66	46
TZP	90	90	TZP	82	72
FOS*	96	NT	FOS	NT	NT
MEM	97	95	MEM	91	88
CIP	65	55	CIP	75	68
Total	n:873	n:198	Total	n:299	n:125

***Non-urine**: CSF (Cerebrospinal Fluid), Blood, DTA (Deep Tracheal Aspirate), Sputum, Wound Culture Samples *: Only for E. coli NT: Not tested*

AN (Amikacin), GN (Gentamicin), AM (Ampicillin), AMC (Amoxicillin/Clavulanic Acid), CRO (Ceftriaxone), FEP (Cefepime), SXT (Trimethoprim/Sulfamethoxazole), TZP (Piperacillin/Tazobactam), FOS (Fosfomycin), MEM (Meropenem), CIP (Ciprofloxacin)

Table 3. Antibiotic Susceptibility Rates of *E. coli* and *K. pneumoniae* Isolates in 2022 (%)

Antibiotic Disk	*E. coli* Urine (%)	*E. coli* Non-urine (%)	Antibiotic Disk	*K. pneumoniae* Urine (%)	*K. pneumoniae* Non-urine (%)
AN	97	93	AN	61	52
GN	86	52	GN	74	62
AM	31	20	AM	4	4
AMC	55	31	AMC	31	13
CRO	92	90	CRO	57	50
FEP	75	51	FEP	65	57
SXT	53	30	SXT	65	44
TZP	90	90	TZP	82	72
FOS*	95	NT	FOS	NT	NT
MEM	97	93	MEM	88	86
CIP	63	54	CIP	72	65
Total	n:1468	n:398	Total	n:419	n:117

***Non-urine**: CSF (Cerebrospinal Fluid), Blood, DTA (Deep Tracheal Aspirate), Sputum, Wound Culture Samples *: Only for E. coli NT: Not tested*

AN (Amikacin), GN (Gentamicin), AM (Ampicillin), AMC (Amoxicillin/Clavulanic Acid), CRO (Ceftriaxone), FEP (Cefepime), SXT (Trimethoprim/Sulfamethoxazole), TZP (Piperacillin/Tazobactam), FOS (Fosfomycin), MEM (Meropenem), CIP (Ciprofloxacin)

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ACADEMIC JOURNAL OF HEALTH

ORIGINAL ARTICLE

Periprosthetic Distal Femur Fractures: A Single-Center Retrospective Epidemiological Analysis

ABSTRACT

Background and Aims: Distal femur fractures (DFFs) are relatively rare but clinically significant injuries associated with high morbidity and mortality. With the rising prevalence of total knee arthroplasty (TKA), the proportion of periprosthetic distal femur fractures (PPDFFs) has been increasing. The incidence, classification, and clinical characteristics of DFFs, with a particular focus on PPDFFs, were aimed to be evaluated in this study.

Methods: Patients admitted to our tertiary care trauma center between January 2020 and 2025 with a diagnosis of distal femur fracture were included in this retrospective descriptive study. Demographic data, mechanism of injury, fracture classification, treatment preference, surgical approach, recorded complications, and comorbidities were analyzed.

Results: A total of 56 patients were evaluated, including 46 (82.1%) with native DFFs and 10 (17.9%) with PPDFFs following TKA or Total hip arthroplasty (THA) . Female predominance was significantly higher in the PPDFF group compared to native fractures (100% vs. 63%, p=0.023). All PPDFFs resulted from simple falls (100%), whereas the native group had a more diverse trauma profile (p=0.036). Fracture type, Charlson Comorbidity Index and postoperative complication rates were similar between groups (p=0.702, p=0.170, p=0.639, respectively).

Conclusion: PPDFFs constituted 17.9% of all DFFs in our series, aligning with reports from tertiary referral centers. These injuries predominantly affect elderly women and are strongly associated with low-energy falls. The findings underscore the need for preventive strategies such as osteoporosis management and fall prevention, as well as for timely surgical intervention and updated epidemiological data to optimize treatment planning and improve outcomes.

Keywords: Distal femur fracture; periprosthetic fracture; total knee arthroplasty; epidemiology; AO/OTA classification; Rorabeck classification; Vancouver classification

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Introduction

Distal femur fractures (DFFs) exhibit a bimodal distribution, typically occurring due to low-energy trauma in elderly patients and high-energy mechanisms in younger individuals (1). Such injuries, particularly those involving complex intra-articular extension, pose significant management challenges and are associated with elevated morbidity and mortality rates (2). The challenge is further compounded by the complex anatomy of the distal femur and the presence of high-energy deforming forces (3). To facilitate precise classification and improved treatment planning, the Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association (AO/OTA) classification system categorizes these fractures into three distinct types based on the extent of articular involvement: Type A (extra-articular), Type B (partial articular), and Type C (complete articular) (4). Historically, locking plates and intramedullary nails have been the most prevalent fixation methods preferred. However, in recent years, the combined use of both implants has gained popularity due to their potential biomechanical advantages and improved clinical outcomes (5,6).

With the increasing frequency of total joint arthroplasty procedures, the prevalence of periprosthetic distal femur fractures (PPDFFs) has also increased. (7,8). The classification of PPDFFs, particularly those occurring in the setting of total knee arthroplasty, is typically performed using both the AO/OTA and Lewis–Rorabeck

classification systems. (9). The Lewis–Rorabeck classification was utilized for the categorization of fractures following total knee arthroplasty, distinguishing between non-displaced fractures with stable implants (Type I), displaced fractures with stable implants (Type II), and fractures associated with a loose or failing prosthesis (Type III).The classification is predicated on two principal factors: the stability of the prosthesis and the displacement of the fracture. It is noteworthy that the majority of PPDFFs following total knee arthroplasty have been categorized as Rorabeck Type II in the literature, signifying displaced fractures with a stable implant (11). As demonstrated in the extant literature, the treatment principles for PPDFFs are analogous to those utilized in the management of native DFFs. The treatment of PPDFFs typically involves the use of locking plates or intramedullary nailing (10).

Despite the growing awareness of distal femoral injuries, there is a paucity of data regarding the proportion of periprosthetic fractures among all DFFs in clinical practice. In light of the aging population and the increasing prevalence of arthroplasty operations, updated epidemiological data are imperative in order to inform treatment strategies.To address this research gap, the incidence and distribution of DFFs in a tertiary care trauma center between 2020 and 2025 were analyzed. The study focuses in particular on the proportion, classification and clinical characteristics of periprosthetic cases.

Methods

Study population and data collection

This retrospective descriptive study was conducted in the Department of Orthopaedics and Traumatology at ** Hospital. Patients diagnosed and treated for DFFs between January 2020 and 2025 were included in the present evaluation. All patients with DFFs who underwent treatment and subsequent follow-up at our clinic were included in the study, irrespective of the treatment method applied.Patients with pathological fractures, patients younger than 18 years, and those with incomplete clinical or radiological data were excluded from the study. A total of 56 patients were identified, of whom 46 presented with native DFFs and 10 sustained PPDFFs following total knee or hip arthroplasty.

The present study was conducted in accordance with the principles of the Declaration of Helsinki, with ethical approval obtained from the local institutional review board (Approval No: E1-22-2905) and informed consent waived due to the retrospective design.

Evaluation of the Patients

Patients were identified retrospectively through a systematic review of the hospital's electronic medical records and clinical archives. The collected data comprised demographic characteristics (age, gender, side of fracture), mechanism of injury, comorbidities, fixation methods, preferred surgical approach, and postoperative complications.

The classification of fractures was conducted in accordance with the AO/OTA system, which was utilized for the categorization of DFFs. In the periprosthetic subgroup, additional classification systems were applied depending on the primary implant. The Lewis–Rorabeck classification was utilized for the categorization of fractures following TKA. The Vancouver classification was utilized for fractures following total hip arthroplasty, wherein DFFs are categorized as Type C—fractures occurring well distal to the femoral stem—with subsequent subcategorization (Types C1–C3) based on implant stability and the quality of the surrounding bone stock. The mechanism of injury (simple fall, high-energy fall, traffic accident, gunshot wound) was documented for each case.

The evaluation of comorbidity was conducted utilizing the Charlson Comorbidity Index (CCI), a system of validation that predicts a 10-year mortality risk based on the presence and severity of chronic diseases. These diseases include, but are not limited to, diabetes, cardiovascular, pulmonary, renal, hepatic, and malignant conditions. Higher CCI scores have been demonstrated to be a reliable indicator of a greater comorbidity burden and poorer survival.

A comprehensive set of surgical data was meticulously documented, encompassing the fixation methods employed (e.g., plate-screw fixation, intramedullary nailing, cannulated screws, or external fixation) and the surgical approaches utilized (e.g., anterolateral, midline, posteromedial, percutaneous, or combined). In the periprosthetic subgroup, the time from fracture to surgery (in days) and the duration of follow-up (in months) were also documented.

All postoperative local and systemic complications were systematically evaluated and categorized as wound problems, implant failures, peri-implant fractures, and pulmonary thromboembolism (PTE). Mortality was also considered a complication for patients who died during the early postoperative period .

Statistical analysis

SPSS version 25.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. Categorical variables were represented by frequencies and percentages, while continuous variables were represented by median and minimum-maximum values. The Kolmogorov–Smirnov test was used to determine whether the continuous data's distribution was normal or skewed. For group comparisons, as all continuous data were skewedly distributed, the Mann–Whitney U test was utilized. The Chi-square Test and the Fisher's Exact Test (when the Chi-square assumption was not met) were used to assess categorical data (gender, side, injury mechanism, fixation method, surgical approach, classification, and complications). P-values less than 0.05 were regarded as statistically significant.

Results

A total of 56 patients were included in the study, consisting of 46 native DFFs (82.1%) and 10 PPDFFs (17.9%). The mean age was 69.5 years (18–88) in the native group and 74.5 years (56–

94) in the periprosthetic group, with no statistically significant difference (p=0.235). Female predominance was noted in both groups; however, all periprosthetic fractures occurred in women (100%), compared with 63% in the native group (p=0.023). The mechanism of injury differed significantly between groups: while all PPDFFs (100%) resulted from low-energy simple falls, native DFFs demonstrated a more heterogeneous trauma profile, including simple falls (60.9%), high-energy falls (19.6%), traffic accidents (13%), and gunshot wounds (6.5%) (p = 0.036). Detailed distribution of the demographic and surgical variables is shown in Table 1.

Within the PPDFFs, 80% of fractures occurred following TKA and 20% after THA. TKA-related fractures were most frequently classified as Lewis–Rorabeck type II (62.5%), followed by type I (25%) and type III (12.5%). The two THA-related fractures were categorized as Vancouver C2 (50%) and C3 (50%) (Table 2).

In terms of surgical treatment, the majority of patients in both groups underwent plate-screw fixation (87% in the native group vs. 80% in the periprosthetic group, p=0.276). No patient with PPDFF underwent revision arthroplasty operation. The anterolateral approach was the most frequently used surgical approach in both groups (82.6% in native vs. 60% in periprosthetic), followed by the midline incision (10.9% vs. 20%), with other approaches being rarely used; no significant difference was detected (p=0.119) (Table 1).

Postoperative complications showed a different profile between groups. The periprosthetic group demonstrated wound complications in 30% of patients but no implant failure, peri-implant fracture, or mortality were recorded during the follow-up. Overall complication rates were not statistically different between the two groups (p=0.639).

Discussion

Although distal femur fractures account for less than 1% of all fractures, they are of considerable clinical importance due to the significant morbidity and mortality (12). Martinet et al. initially reported this rarity, and Elsoe et al. later confirmed the low overall incidence in a large population-based study, while also emphasizing the considerable clinical burden associated with these injuries (13). The proportion of periprosthetic fractures among DFFs is steadily increasing (14). In light of the aging population and the increasing prevalence of arthroplasty operations, updated epidemiological data are imperative. The significance of our study lies in reporting the 5-year results of our tertiary trauma center, while also highlighting the epidemiological differences between PPDFF and native fractures. In the present study, periprosthetic fractures constituted 17.9% of all DFFs. The most striking finding of the study was the significantly higher prevalence of PPDFFs in the female population, with these cases almost always observed following simple falls.

PPDFFs accounted for 17.9% of all DFFs in this series, which is lower than 28.7% that was reported in the population-based Danish study by Elsoe et al. (13). Several factors may explain this discrepancy, including differences in study design (single-center vs. population-based), demographic characteristics, regional prevalence of total knee arthroplasty, and data collection periods. It is also possible that local variations in implant longevity and revision rates have influenced the observed proportion of periprosthetic cases. In line with this, Direder et al. reported that the incidence of PPDFFs ranges from 0.3% to 2.5% after primary TKA and increases up to 38% following revision procedures, highlighting the influence of study design and case variations on reported proportions (15).

In the light of an aging population and the rising incidence of high-energy trauma among younger individuals, DFFs have garnered increasing attention in the orthopedic literature. Khan et al., in their five-year epidemiological analysis from a central London major trauma center, highlighted this characteristic bimodal distribution, with high-energy trauma predominating in younger patients and low-energy falls in the elderly (16). The present study provided updated epidemiological data on distal femur fractures and demonstrated the contribution of DFFs within the context of this increasing trend. A marked female predominance was noted in the PPDFF group (100%) compared to the native DFF group (63%), (p=0.023). This finding is consistent with previous reports highlighting that elderly women are at increased risk for PPDFFs, likely due to the combined effects of osteoporosis, lower bone mineral density, and the higher incidence of primary TKA in this population (17). Recent evidence further supports this association: Park et al. demonstrated that osteoporosis significantly increases the risk of PPDFFs after TKA, particularly in elderly women with untreated bone fragility (18). Similarly, Houel et al. reported that patients sustaining periprosthetic femoral fractures are typically older adults with a high prevalence of osteoporosis (19). In addition, Mazur et al. found that nearly 90% of PPDFF cases in their series occurred in women, underscoring the combined influence of sex-specific bone quality and implant-related factors (20). The strong female predominance is also in line with the fact that low-energy trauma was the exclusive mechanism of injury in the PPDFF group, further supporting the role of fragility and implant-related factors in fracture pathogenesis. Furthermore, all periprosthetic cases in this study resulted from low-energy falls, whereas high-energy trauma, including falls from height, traffic accidents, and gunshot wounds, occurred exclusively in the native group. This distribution aligns with the bimodal injury pattern described in previous epidemiological studies (13,16), in which native fractures occur both after low-energy falls in the elderly and high-energy trauma in younger patients. Moreover, these findings are consistent with Al-Jabri et al., who reported that the vast majority of PPDFFs around total knee replacements result from low-energy mechanisms, with high-energy trauma being relatively uncommon (21).

The management of DFFs requires advanced surgical expertise and the application of sound biomechanical principles. As

emphasized by Nauth et al., DFFs demand meticulous surgical technique and adherence to biomechanical principles to optimize fixation stability and reduce complication rates (22). Moreover, Quinzi et al. emphasized that surgical management—most commonly locking plate fixation, retrograde intramedullary nailing, or distal femoral replacement—provides more reliable outcomes than conservative treatment, which is associated with high rates of nonunion, malunion, and reoperation (23). In our series, plate-screw fixation was the predominant surgical method, both in native (87%) and PPDFFs (80%). This trend reflects the widespread adoption of locked plating systems in elderly, osteoporotic patients and in the presence of knee or hip prostheses, where intramedullary nailing may be technically challenging (24). Nevertheless, intramedullary nailing remains a valuable alternative in selected cases. A recent systematic review by Shah et al. demonstrated equivalent union rates between intramedullary nails and locked plate fixation for PPDFFs, emphasizing that implant choice should be individualized according to fracture pattern, bone quality, and prosthesis design (25).

Periprosthetic fractures tended to occur in older patients and required a greater variety of surgical approaches compared to native fractures, reflecting the influence of prior prosthetic surgery and soft tissue scarring on surgical exposure. Interestingly, implant failure was observed only in native fractures, while wound-related complications predominated in the periprosthetic group, suggesting that the complication profile differs between these entities. Furthermore, the relatively high proportion of 33B2 fractures in the periprosthetic cohort (8.7% vs. 30%) emphasizes the susceptibility of the metaphyseal region adjacent to prosthetic implants. Wound complications were more frequent in PPDFFs (30%) compared to native cases (17.4%). This observation is consistent with recent reports indicating higher rates of wound-related problems in periprosthetic fractures, attributed to advanced patient age, multiple comorbidities, and compromised soft tissue integrity following prior arthroplasty (15,26).

Several limitations should be acknowledged. The retrospective design of the study may have resulted in the creation of selection bias, thereby hindering the establishment of causal relationships. The relatively limited sample size of the periprosthetic group is a particular concern, as it restricts the statistical power and generalizability of the findings. The single-center nature of the study may limit its ability to generalize the findings to other institutions. The evaluation of functional outcomes and patient-reported measures was not conducted, and the shorter follow-up period may have resulted in an underestimation of late complications, such as nonunion or implant failure. In order to enhance the generalizability of the findings, prospective multicenter studies involving larger patient cohorts are required in order to validate the results. It is recommended that future research endeavors focus on the identification of independent risk factors for PPDFFs. This finding has the potential to inform the development of targeted prevention strategies and optimized management protocols.

CONCLUSION

PPDFFs are a distinct fracture group that should be considered separately from native DFFs. In the present series, they accounted for 17.9% of all DFFs, a significantly higher incidence of which has been observed in women and which occurs following almost always low-energy trauma associated with fragility. The high incidence of wound complications in this group, although not statistically significant, underscores the challenges associated with treatment and the importance of meticulous soft tissue management.

Conflicts of interest: The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript

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Ethical approval: This study was reviewed and approved by the Bilkent City Hospital, Non-Pharmaceuticals and Non-Medical Devices Research Ethics Committee (Approval No: E1-22-2905).

Consent to Participate: Informed consent was not required because of the retrospective design of the study.

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Tables

Table 1: Comparing demographics of native and periprosthetic distal femur fractures

		Native (n=46)	**Periprosthetic** (n=10)	**P**
Age (years)		69.5 (18-88)	74.5 (56-94)	0.235
Gender	**Female**	29 (63%)	10 (100%)	***0.023***
	Male	17 (37%)	0	
Side	**Right**	33 (71.7%)	9 (90%)	0.423
	Left	13 (28.3%)	1 (10%)	
Injury Mechanism	**Simple Fall**	28 (60.9%)	10 (100%)	***0.036***
	High-Energy Fall	9 (19.6%)	0	
	Traffic Accident	6 (13%)	0	
	Gunshot Wound	3 (6.5%)	0	
Fixation Technique	**Plate-Screw Fixation**	40 (87%)	8 (80%)	0.276
	Cannulated Screws	4 (8.7%)	1 (10%)	
	External Fixator	2 (4.3%)	0	
	Intramedullary Nail	0	1 (10%)	
Surgical Approach	**Anterolateral**	38 (82.6%)	6 (60%)	0.119
	Midline	5 (10.9%)	2 (20%)	
	Medial/Posteromedial	1 (2.2%)	1 (10%)	
	Percutaneous	2 (4.3%)	0	
	Combined	0	1 (10%)	
AO Classification	**33A1**	2 (4.3%)	1 (10%)	0.702
	33A2	13 (28.3%)	2 (20%)	
	33A3	10 (21.7%)	1 (10%)	
	33B1	2 (4.3%)	0	
	33B2	4 (8.7%)	3 (30%)	
	33B3	3 (6.5%)	0	
	33C1	3 (6.5%)	1 (10%)	
	33C2	4 (8.7%)	1 (10%)	
	33C3	5 (10.9%)	1 (10%)	
Complications	**None**	24 (52.2%)	7 (70%)	0.639
	Wound Problem	8 (17.4%)	3 (30%)	
	Implant Failure	5 (10.9%)	0	
	Exitus	7 (15.2%)	0	
	Periimplantic Fracture	1 (2.2%)	0	
	PTE	1 (2.2%)	0	
Charlson Comorbidity Index		4 (0-7)	4 (0-7)	0.170

n: number of patients, PTE: pulmoner thromboembolism

Table 2: Detailed demographic profile of the periprosthetic distal femur fractures

		Number of Patients (%) (N=10)
Age (years)		74.5 (56-94)
Gender	**Female**	10 (100%)
	Male	0
Side	**Right**	9 (90%)
	Left	1 (10%)
Injury Mechanism	**Simple Fall**	10 (100%)
Primary Implant	**Total Knee Arthroplasty**	8 (80%)
	Total Hip Arthroplasty	2 (20%)
Fracture Type – Primary Total Knee Arthroplasty (n=8)	**Lewis-Rorabeck Type 1**	2 (25%)
	Lewis-Rorabeck Type 2	5 (62.5%)
	Lewis-Rorabeck Type 3	1 (12.5%)
Fracture Type – Primary Total Hip Arthroplasty (n=2)	**Vancouver Type C2**	1 (50%)
	Vancouver Type C3	1 (50%)
Fixation Technique	**Plate-Screw Fixation**	8 (80%)
	Cannulated Screws	1 (10%)
	Intramedullary Nail	1 (10%)
Surgical Approach	**Anterolateral**	6 (60%)
	Midline	2 (20%)
	Medial/Posteromedial	1 (10%)
	Combined	1 (10%)
Follow-up (months)		6 (6-17)
Duration between Fracture to Surgery (days)		5 (0-21)
Complications	**None**	7 (70%)
	Wound Problem	3 (30%)

n: number of patients

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ACADEMIC JOURNAL OF HEALTH

ORIGINAL ARTICLE

Comparative Evaluation of Blood Gas and Biochemistry Analyzers in Lactate Measurement in Pediatric Patient Groups

ABSTRACT

Objective

Lactate is an early biochemical marker of tissue hypoxia and hypoperfusion and plays an important role in clinical decision-making. This study aimed to compare lactate measurements obtained from blood gas and central laboratory biochemistry analyzers in pediatric patients and to evaluate the clinical agreement between the two methods.

Methods

Pediatric patients with simultaneous lactate measurements performed on blood gas and biochemistry analyzers at the Ankara Etlik City Hospital Medical Biochemistry Laboratory between January 2023 and August 2025 were retrospectively reviewed. A total of 914 paired lactate measurements were included. Method comparison was performed using Pearson correlation, Bland–Altman analysis, Passing–Bablok regression, and Cohen's kappa coefficient. A total allowable error (TEa) of ±0.20 mmol/L was used as the clinical acceptance criterion.

Results

A very strong positive correlation was observed between blood gas and biochemistry measurements ($r = 0.95$, $p < 0.0001$). Bland–Altman analysis showed a mean bias of −0.13 mmol/L (95% CI: −0.18 to −0.08), with limits of agreement (LoA) from −1.56 to 1.31 mmol/L; 95.1% of results fell within these limits. Passing–Bablok regression yielded $y = 0.211 + 0.975x$ (intercept 0.211, 95% CI: 0.168–0.251; slope 0.975, 95% CI: 0.954–0.996), with no deviation from linearity (CUSUM $p = 0.97$). Categorical agreement was substantial ($\kappa = 0.73$, 95% CI: 0.70–0.76), and misclassification remained below 10%.

Conclusion

Blood gas and biochemistry analyzers demonstrated a high level of agreement for lactate measurement in pediatric patients. The rapid turnaround time of blood gas analyzers may support timely clinical decision-making, particularly in emergency and intensive care settings. Although minor differences were observed at low and high concentrations, these were not large enough to meaningfully affect clinical interpretation.

Keywords: blood gas analysis; inter-device variability; lactate

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Introduction

Lactate is a key end product of cellular metabolism and increases particularly under anaerobic conditions. In clinical practice, lactate serves as an early indicator of tissue hypoxia and hypoperfusion and provides prognostic information in sepsis, septic shock, cardiac arrest, trauma, and other critical illnesses (1,2). In pediatric patients, lactate monitoring plays an important role not only in diagnosis but also in assessing response to treatment and predicting mortality risk (3). Children have distinct physiological characteristics—such as higher metabolic rates, age-dependent lactate clearance, and variable oxygen consumption—that may influence lactate kinetics compared with adults. Clinically used decision thresholds (<2 mmol/L, ≥2 mmol/L, and ≥4 mmol/L) are therefore highly relevant in pediatric emergency and intensive care settings due to their association with disease severity and outcomes (1–3).

In clinical laboratories, lactate is commonly measured in plasma using enzymatic methods on central laboratory biochemistry analyzers. These methods are generally regarded as reference approaches due to their accuracy and analytical reliability;

however, sample processing and transport may delay reporting (4). In contrast, point-of-care blood gas analyzers can provide lactate results within minutes from arterial or venous whole blood, which is particularly valuable in emergency and intensive care units where rapid decisions are required (5). Despite this advantage, methodological and matrix differences between whole-blood and plasma measurements necessitate method-comparison studies to ensure interchangeability and consistent clinical interpretation (6).

Several studies have compared blood gas analyzers with central laboratory analyzers, highlighting overall agreement but also potential systematic or proportional bias, especially around clinically important thresholds (7). However, most evidence has been generated in adult or mixed populations, while pediatric-specific data remain limited. Because lactate physiology and variability differ in children, this gap may introduce uncertainty in pediatric practice.

Accordingly, the aim of this study was to compare lactate measurements obtained using blood gas and biochemistry analyzers in pediatric patients and to evaluate clinical agreement between the two methods. By doing so, we sought to support the safe use of blood gas lactate in pediatric care and contribute to the literature on the clinical utility of point-of-care testing.

Methods

Study Design

This retrospective study evaluated data from the Medical Biochemistry Laboratory of Ankara Etlik City Hospital between January 1, 2023, and August 1, 2025. Pediatric cases in which lactate was measured simultaneously using a blood gas analyzer and a central laboratory biochemistry analyzer were included. Data were retrieved from the Laboratory Information System (LIS). A total of 914 paired lactate measurements were analyzed.

Inclusion criteria were: (i) age 0–18 years, (ii) simultaneous lactate measurements on both analyzers during the study period, and (iii) complete sample data. Exclusion criteria were: age >18 years, results available from only one analyzer, incomplete/incorrect records, a time interval ≥1 hour between paired measurements, and samples with hemolysis, clots, insufficient volume, analyzer error flags, or other rejection criteria. If multiple measurements were available for the same patient, only the first paired result was included.

Measurements

Central laboratory lactate was measured in plasma on two Roche Cobas c702 biochemistry analyzers (Roche Diagnostics, Mannheim, Germany) using the manufacturer's enzymatic colorimetric assay. Blood samples were collected into sodium fluoride (NaF) tubes (BD Vacutainer, Becton, Dickinson Company, Franklin Lakes, NJ, USA), transported on ice packs, and processed according to local protocols to minimize in vitro glycolysis.

Blood gas lactate was measured at the point of care using four Siemens RAPIDPoint 500 analyzers from heparinized arterial or venous whole blood, in accordance with the manufacturer's instructions. Internal quality control (two levels per run) and participation in external quality assessment were in place for the biochemistry analyzers. Blood gas analyzers underwent routine daily multi-point calibration and internal checks according to standard procedures.

Ethics

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Ankara Etlik City Hospital (Approval No: AEŞH-BADEK1-2025-492, Date: 03/09/2025). Informed consent was waived due to the retrospective design and the use of de-identified data.

Statistical Analysis

Method comparison followed CLSI EP09-A3 principles (8). The association between methods was evaluated using Pearson's correlation coefficient ($p < 0.05$ considered significant). Agreement was assessed using Bland–Altman analysis, calculating mean bias and 95% limits of agreement (LoA). Differences were defined as blood gas − biochemistry, and the proportion of paired results within the LoA was reported. Heteroscedasticity was visually assessed on the Bland–Altman plot.

Systematic and proportional differences were evaluated using Passing–Bablok regression, and deviation from linearity was assessed using the cumulative sum (CUSUM) test. The TEa for lactate published by the Wisconsin State Laboratory of Hygiene (WSLH) was used as the clinical acceptance criterion (±0.20 mmol/L) (9). Predicted differences at the 2 mmol/L and 4 mmol/L decision points were calculated from the regression equation and compared against this acceptance limit.

For categorical agreement, lactate values were grouped as <2 mmol/L, 2–4 mmol/L, and >4 mmol/L. Cohen's kappa (κ) with 95% CI was calculated. Misclassification rates at the >2 mmol/L and >4 mmol/L thresholds were also reported. A $\kappa \geq 0.70$ was interpreted as good agreement (10). All analyses were performed using MedCalc 23.3.5 (MedCalc Software Ltd, Ostend, Belgium).

Results

In the biochemistry analyzer dataset, the median lactate concentration was 1.84 mmol/L (IQR: 1.31–2.92), with 2.5th and 97.5th percentiles of 0.73 and 9.63 mmol/L, respectively. In the blood gas dataset, the median was 2.02 mmol/L (IQR: 1.49–2.99), with corresponding percentiles of 0.93 and 9.80 mmol/L. Most measurements clustered within the lower clinical range. In the biochemistry dataset, 14.6% (134/914) of results were ≥4 mmol/L, compared with 13.3% (122/914) in the blood gas dataset.

A very strong positive correlation was observed between methods ($r = 0.95$, $p < 0.0001$). Bland–Altman analysis showed a mean bias of −0.13 mmol/L (95% CI: −0.18 to −0.08), indicating that blood gas results were slightly lower on average. The LoA ranged from −1.56 mmol/L (95% CI: −1.64 to −1.48) to 1.31 mmol/L (95% CI: 1.23 to 1.39), and 869/914 (95.1%) paired results fell within these limits (Figure 1). No clear increase in dispersion at higher lactate concentrations was observed.

Passing–Bablok regression yielded $y = 0.211 + 0.975x$ (y: blood gas; x: biochemistry), with an intercept of 0.211 (95%

CI: 0.168–0.251) and a slope of 0.975 (95% CI: 0.954–0.996) (Table 1). The CUSUM test showed no deviation from linearity (p = 0.97) (Figure 2). According to the model, equal values were predicted at approximately 8.4 mmol/L, with blood gas results slightly higher below this point and biochemistry results slightly higher above it.

At the clinical decision thresholds, the regression-derived predicted bias was 0.164 mmol/L (95% CI: 0.076–0.243) at 2 mmol/L and 0.112 mmol/L (95% CI: −0.016–0.235) at 4 mmol/L; both were within the predefined TEa of ±0.20 mmol/L.

When assessed against TEa (±0.20 mmol/L), 38.8% (355/914) of paired measurements fell within this analytical performance criterion. In categorical analysis, agreement was substantial (κ = 0.73, 95% CI: 0.70–0.76). Misclassification at the >2 mmol/L and >4 mmol/L thresholds remained below 10%, indicating good clinical concordance.

Discussion

This study compared lactate measurements obtained using blood gas and central laboratory biochemistry analyzers in pediatric patients. Overall, the methods showed strong correlation and clinically acceptable agreement. Bland–Altman analysis demonstrated a small negative mean bias (−0.13 mmol/L), and Passing–Bablok regression supported a linear relationship without clinically meaningful constant or proportional bias.

Previous studies comparing point-of-care analyzers with central laboratory methods have generally reported high correlation but have also noted that analyzer-specific biases may be more evident at very low or very high lactate concentrations (11–14). Our findings are consistent with this literature and extend it by providing pediatric-specific evidence using simultaneous measurements across Roche Cobas c702 and Siemens RAPIDPoint platforms.

Minor differences between analyzers may reflect methodological and matrix differences. Central laboratory analyzers typically measure lactate in plasma using enzymatic colorimetric methods, whereas blood gas analyzers measure lactate in whole blood using electrochemical methods. Preanalytical factors (e.g., sampling, processing time, and in vitro glycolysis) may further contribute to observed differences. Despite these sources of variability, the key clinical advantage of blood gas analyzers is their rapid turnaround time, which can support urgent clinical decisions in emergency and intensive care settings.

Although TEa was set narrowly at ±0.20 mmol/L, predicted biases at the clinically relevant 2 mmol/L and 4 mmol/L thresholds remained within this acceptance limit. Moreover, categorical agreement was substantial, and misclassification rates were low, suggesting that method-related differences are unlikely to meaningfully alter clinical classification at these decision points. The intersection predicted near 8.4 mmol/L appears to be an analytical feature of the regression model rather than a clinically meaningful threshold, particularly because pediatric decision-making is often concentrated in the lower lactate range.

Strengths of this study include the pediatric-only population, large sample size, and simultaneous paired measurements. Limitations include the retrospective design, limited control over preanalytical variables, potential inter-device variability due to multiple analyzers, and the use of different sample matrices (whole blood vs plasma). In addition, the single-center design may limit generalizability. Nevertheless, the findings provide clinically useful evidence supporting the use of blood gas lactate in pediatric practice.

Conclusıon

Blood gas and central laboratory biochemistry analyzers showed a high degree of agreement in lactate measurements in pediatric patients. The rapid availability of results from blood gas analyzers represents an important advantage in emergency and intensive care settings. Although small methodological differences may occur, particularly at extreme concentrations, agreement at clinically relevant decision thresholds was acceptable. Further prospective and multi-center studies may support standardization and strengthen evidence for pediatric clinical decision-making.

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None.

Author Contributions

All authors approved the final manuscript. The manuscript has not been published in whole or in part and is not under consideration elsewhere.

Conflict of Interest

The authors declare no conflicts of interest.

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Tables

Table 1. Passing-Bablok regression analysis

Parameter	Passing-Bablok Regression	Intercept (95% CI)	Slope (95% CI)	Cusum test for linearity
Lactate	y = 0.211 + 0.974. x	0.168 – 0.251	0.954 – 0.996	No significant deviation from linearity (P=0,97)

The regression equation describes the relationship between blood gas (y) and biochemistry (x) lactate measurements. CI = confidence interval; Cusum = cumulative sum test.

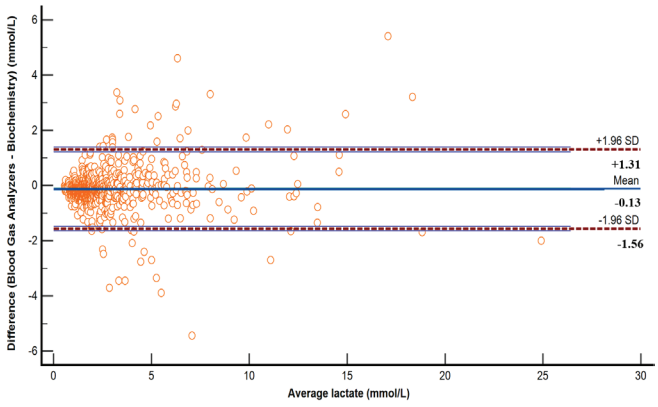

Figure 1. Bland–Altman plot comparing lactate measurements obtained from the blood gas and the biochemistry analyzers. The solid line indicates the mean bias (−0.13 mmol/L; 95% CI: −0.18 to −0.08), while the dashed lines represent the 95% LoA (−1.56 to +1.31 mmol/L; 95% CI: −1.64 to −1.48 and 1.23 to 1.39, respectively). The blue lines surrounding each LoA represent the 95% CI of the LoA estimates. A total of 869 out of 914 paired results (95.1%) were within the LoA.

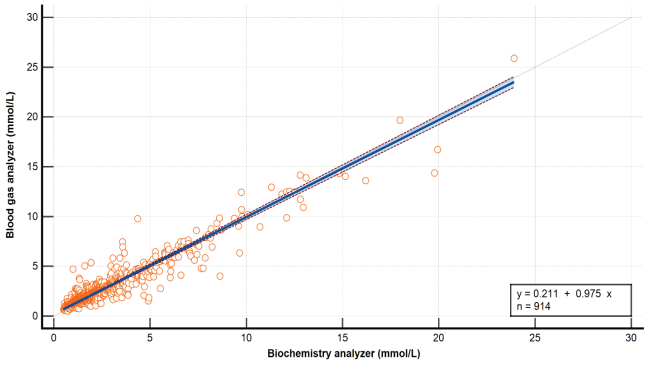

Figure 2. Passing–Bablok regression analysis comparing lactate measurements obtained from the blood gas analyzers (y-axis) and the biochemistry analyzers (x-axis).

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ACADEMIC JOURNAL OF HEALTH

CASE REPORT

Life-Threatening Iliac Artery Injury During Lumbar Discectomy: Successful Management with Massive Transfusion

ABSTRACT

Major vascular injury during lumbar discectomy is a rare but potentially fatal complication, with an incidence of 0.01–0.05%. We present a 49-year-old female with systemic lupus erythematosus who developed hemorrhagic shock due to a common iliac artery injury during single-level lumbar discectomy. The patient experienced sudden hypotension and tachycardia intraoperatively. Emergency laparotomy revealed a 6500 mL blood loss; massive transfusion protocol was initiated, and the artery was repaired with a Dacron graft. A total of 11 units of red blood cells, 2 units of platelets, 6 units of cryoprecipitate, and 6 units of plasma were transfused. The patient stabilized postoperatively and was discharged without neurological deficit on day 12. This case highlights the importance of early recognition, rapid multidisciplinary intervention, and massive transfusion in the management of major vascular injuries during lumbar discectomy to improve patient outcomes.

Keywords: vascular injury, iliac artery, lumbar discectomy

Introduction

Lumbar discectomy via a posterior approach is a common neurosurgical procedure. Although rare, life-threatening iatrogenic vascular injuries may occur, particularly if not recognized early [1,2]. The reported incidence of vascular injury during lumbar discectomy ranges from 0.01% to 0.05% [3]. These injuries may involve the aorta, inferior vena cava or iliac vessels, and can result in arteriovenous fistulas (AVFs), pseudoaneurysms or deep vein thrombosis (DVT). Reported mortality rates range from 15% to 65% [1,3-5]. We report a case of right common iliac artery injury during single-level lumbar discectomy that was successfully managed through prompt diagnosis, implementation of a massive transfusion protocol and open surgical repair.

Case Presentation

A 49-year-old female with systemic lupus erythematosus receiving chronic corticosteroid therapy (ASA II) was scheduled for a single-level lumbar discectomy under spinal anesthesia. Perioperative stress-dose corticosteroids were administered. During surgical hemostasis, at approximately 60 minutes after incision, the patient developed sudden hypotension, agitation and tachycardia. A major vascular injury was suspected, and the surgical site was closed immediately. The patient was repositioned to the supine position.

After endotracheal intubation, an emergency laparotomy revealed an injury to the right common iliac artery. Cardiovascular surgeons were consulted immediately. Central venous catheterization and invasive arterial blood pressure monitoring were established. A continuous noradrenaline infusion was started because of persistent hemodynamic instability.

Arterial blood gas analysis showed hemoglobin 3.5 g/dL, hematocrit 10%, ionized calcium 0.68 mmol/L, total calcium 6.18 mg/dL, lactate 6.84 mmol/L and pH 7.15. The estimated blood loss was calculated from the suction canister volume after subtracting irrigation fluids, together with the number and saturation of surgical sponges and

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laparotomy pads, and was approximately 6500 mL. A massive transfusion protocol was therefore initiated.

In total, the patient received 11 units of packed red blood cells, 6 units of fresh frozen plasma, 6 units of cryoprecipitate and 2 units of apheresis platelets over a period of 4 hours, corresponding to an average transfusion rate of approximately 1625 mL/h. Vascular repair was performed using a Dacron graft. Following repair, the patient's hemodynamic status stabilized, and noradrenaline was gradually weaned off. The total surgical time was 5.5 hours. She was transferred intubated to the intensive care unit (ICU). She was extubated 5 hours postoperatively. Arterial doppler ultrasound performed on postoperative days 2 and 7 revealed normal blood flow in both lower extremities. The patient remained hemodynamically stable and was discharged on postoperative day 12 without neurological deficits and with aspirin therapy. Postoperative computed tomography images demonstrated the repaired right common iliac artery. (Figure 1 and Figure 2).

Discussion

Although infrequent, major vascular injuries during lumbar discectomy are associated with considerable morbidity and mortality [1,4]. The aorta and iliac vessels lie directly anterior to the intervertebral disc space, particularly at the L4–L5 and L5–S1 levels, where the anterior longitudinal ligament is relatively thin [2]. Inadvertent penetration of this ligament during disc removal may result in catastrophic bleeding. Iatrogenic vascular injury typically presents with sudden hypotension, tachycardia or unexpected blood loss, as in our case. However, the diagnosis may be delayed when bleeding is retroperitoneal or the initial injury is limited. Several reports describe patients who developed symptoms hours or even days after the procedure, manifesting as abdominal distension, limb swelling, arteriovenous fistula or pseudoaneurysm formation [4–7]. Early intraoperative recognition, as occurred in our patient, is critical for survival. Rapid closure of the posterior incision, prompt repositioning of the patient and immediate emergency laparotomy provided timely exposure and repair of the injured iliac artery. The massive transfusion protocol, guided by real-time arterial blood gas analysis, was crucial for restoring circulating volume and preventing coagulopathy, acidosis and hypothermia, and met commonly used definitions of massive transfusion (≥10 units of packed red blood cells within 24 hours). Treatment options for these injuries include both open and endovascular techniques. Open surgical repair remains the gold standard in the presence of massive hemorrhage and hemodynamic instability [4]. Endovascular approaches are preferable in hemodynamically stable patients or in delayed presentations. Preventive strategies include preoperative imaging to delineate vascular anatomy and identify possible anomalies, particularly in revision surgeries or in high-risk patients. Careful surgical technique, familiarity with anatomical landmarks and readiness for emergency intervention are essential to minimize risk and improve patient safety [8-10].

In conclusion, early clinical suspicion, rapid diagnosis, activation of a massive transfusion protocol and coordinated multidisciplinary management were key to the favorable outcome in this case. Preoperative anatomical awareness and preparation for rare but potentially catastrophic vascular complications should be integral components of surgical planning for lumbar discectomy.

Limitations:

A limitation of this report is the lack of intraoperative imaging documentation before vascular repair; however, postoperative CT angiography confirmed graft patency.

Conflict of Interest Statement:

The authors declare no conflict of interest.

Funding Statement:

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Presentation:

This case has not been presented at any meeting.

Figures

Figure 1

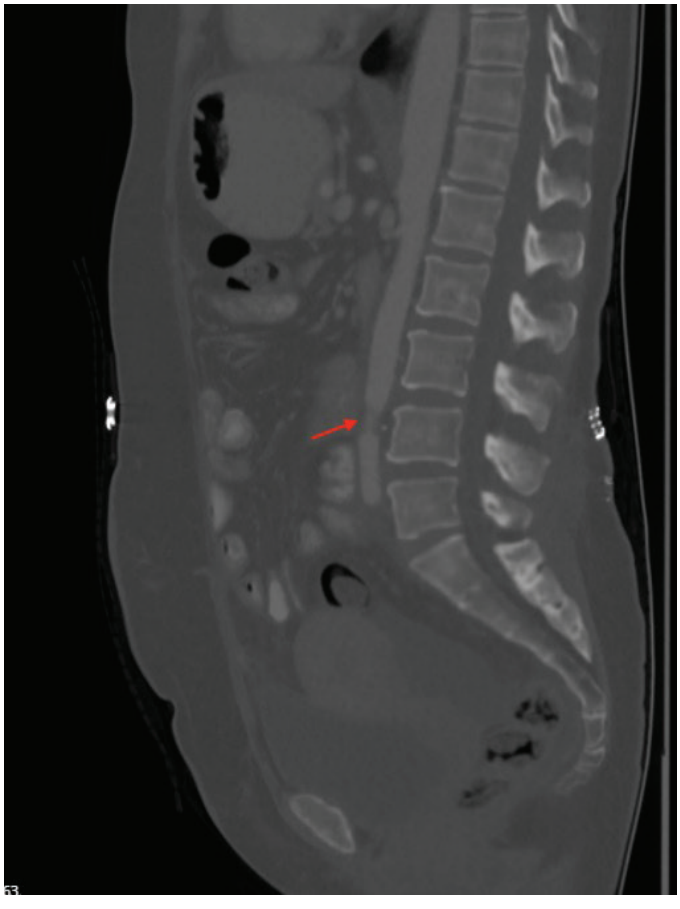
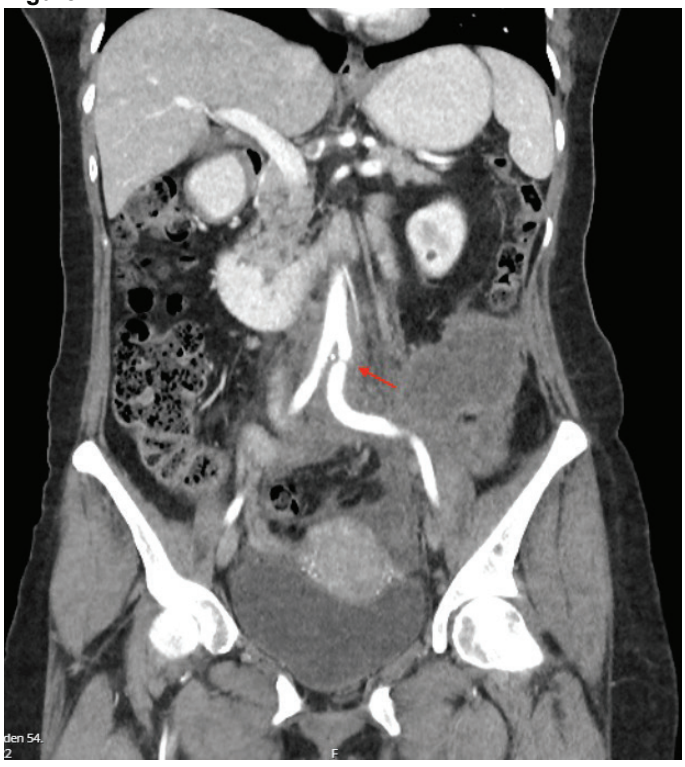


Figure 2



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ACADEMIC JOURNAL OF HEALTH

CASE REPORT

A Rare Cause of Hypercalcemic Crisis in Pregnancy- “Uterine Leiomyoma”

ABSTRACT

Hypercalcemia in pregnancy is a rare condition and causes serious maternal and fetal outcomes. A 35-year-old woman presented with itching, nausea, and vomiting at 37 weeks of spontaneous pregnancy. Biochemical examination revealed hypercalcemia with a low parathyroid hormone (PTH) level and normal 25-hydroxyvitamin D level. An abdominal ultrasound (US) revealed a 158 × 151-mm intramural–subserosal myoma located in the left lateral wall of the uterus. Due to progressive hypercalcemia despite isotonic saline infusion, a single session of hemodialysis was performed. The patient underwent a cesarean section and myomectomy, and normocalcemia was achieved following removal of the placenta and myoma. Parathyroid hormone-related protein (PTHrP) secretion by benign tumors is rare and has been reported in association with intestinal and uterine leiomyomas, as well as renal adenomas.

Keywords: Hypercalcemia, Parathyroid Hormone-related Peptide, Leiomyoma, Uterine

Introduction

Hypercalcemia in pregnancy is a rare condition, with its incidence in women of reproductive age reported to be 0.03% (1,2). The most common cause of hypercalcemia in pregnancy is primary hyperparathyroidism. Other causes, similar to those in the general population, include hyperthyroidism, vitamin A or D toxicosis, familial hypocalciuric hypercalcemia, granulomatous diseases, and malignancies (3,4). Serious maternal outcomes (such as preeclampsia, nephrolithiasis, pancreatitis, and renal failure) and fetal outcomes (including intrauterine growth restriction, abortion, neonatal death, neonatal hypocalcemia, and, rarely, permanent hypoparathyroidism) may occur as a result of hypercalcemia during pregnancy (1,2).

Malignancy-associated hypercalcemia occurs in 20–30% of malignancies and develops through various pathogenetic mechanisms, most commonly due to the release of parathyroid hormone-related protein (PTHrP) (3,4). PTHrP release from benign tumors is quite rare and is referred to as benign tumor–related humoral hypercalcemia (1). Benign tumors that cause PTHrP-mediated hypercalcemia include intestinal and uterine leiomyomas, renal adenomas and benign pheochromocytomas (4). PTHrP release is also physiologically increased during pregnancy, originating from the placenta, breast tissue, and amnion (1).

Here, a 35-year-old pregnant woman was reported who developed hypercalcemic crisis during the third trimester.

Case Presentation

A 35-year-old primigravida at 37 weeks of spontaneous pregnancy was admitted to the gynecology clinic with complaints of itching, nausea, and vomiting for the past week. Her medical records showed Rh incompatibility, polyhydramnios, and a leiomyoma measuring 42 × 32 × 40 mm. On physical examination, vital signs were within the normal range, and there was no vaginal bleeding. Neurological examination revealed no pathological findings. The fetal heart rate was normal. Initial laboratory tests

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revealed a total serum calcium level of 18.8 mg/dL, phosphorus level 2.6 mg/dl at the time of admission. The laboratory data obtained at the time of admission are summarized in Table 1. Retrospective review of the medical records showed that the only available calcium measurement, obtained at 33 weeks' gestation, was 9.03 mg/dl. Serum PTH was 4.4mg/dl. Serum amilase and lipase values were in normal ranges. Calcium oxalate crystals were detected in urine microscopy.

During the assessment for the differential diagnosis of PTH-independent hypercalcemia, we performed a chest X-ray, since organogenesis is completed by the third trimester, Abdominal ultrasonography revealed a 158 × 151 mm intramural–subserosal myoma in the left lateral wall of the uterus. Advanced imaging modalities were not performed because of pregnancy. Due to laboratory limitations, serum PTHrP level could not be measured.

The patient was admitted to the perinatology clinic and was consulted by both the endocrinology and nephrology departments for hypercalcemic crisis. Owing to the progressive increase in serum calcium levels, the patient required transfer to the medical intensive care unit for further evaluation and treatment. Isotonic saline was initiated at a rate of 200 mL/hour, with close monitoring to maintain urine output between 100 and 150 mL/hour.

Due to progressive hypercalcemia, a single session of hemodialysis with low-calcium dialysate was performed on the first day of admission. Following dialysis, the total calcium level decreased to 11.3 mg/dL but subsequently rose again to 17.2 mg/dL on the same day (Figure 1 shows the course of calcium levels).

As the patient was at term and calcium levels could not be stabilized, caesarean delivery and myomectomy were performed on the second day of admission. In the postoperative period, hydration was continued, and calcium levels returned to the normal range within 48 hours. Histopathological examination revealed leiomyoma with degenerative and pregnancy-related changes, without evidence of malignancy and the placenta showed no significant histopathological abnormalities (Figure 2-3). No PTHrP immunohistochemical staining could be carried out on placental or myoma tissue.

Following delivery, both the mother and the newborn remained stable. The newborn's serum calcium level was in normal range. The patient initiated breastfeeding, and the newborn required no medical intervention. They were discharged in the second postpartum week with normal serum calcium levels.

Discussion

We present a rare case of a giant uterine myoma, leading to a hypercalcemic crisis during pregnancy. In the context of pregnancy, the placenta and mammary glands represent the principal sources of PTHrP. Circulating maternal PTHrP concentrations gradually increase throughout gestation and reach their maximum in the third trimester (5). In addition, elevated PTHrP levels may also be observed in association with both malignant and benign tumors (6).

Estrogen and PTHrP contribute to myoma growth, and as the myoma enlarges, PTHrP release further increases (7). Five cases of hypercalcemia during pregnancy associated with leiomyoma have been reported in the literature. These cases are summarized in Table 2. In previously reported cases, PTHrP release was demonstrated either biochemically or by histological staining. In our patient, although PTHrP production could not be confirmed biochemically or histologically in the myoma, placenta, or amnion, serum calcium levels normalized following delivery and myomectomy. Furthermore, imaging studies revealed no alternative source of PTHrP production.

Treatment approaches in such cases are generally similar due to safety concerns during pregnancy. Loop diuretics are associated with placental hypoperfusion and are therefore considered relatively contraindicated (8).

Calcitonin is considered safe in pregnancy, as it does not cross the placenta. However, although fast-acting, it typically lowers serum calcium by only 1–2 mg/dL and is associated with a high risk of tachyphylaxis (9). Cinacalcet is effective only in cases of hypercalcemia associated with elevated PTH levels (7). Bisphosphonates are contraindicated during pregnancy, as they cross the placenta (10).

The cornerstone of treatment for PTHrP-associated hypercalcemia is elimination of the underlying disease. In our case, the probable sources of PTHrP were the myoma and placenta; therefore, their removal represented the main therapeutic approach. Normocalcemia was achieved following removal of the placenta and myoma. Given the advanced gestational age and young maternal age, maternal and neonatal well-being was ensured through successful caesarean section and myomectomy.

Conclusion

When evaluating hypercalcemia during pregnancy, humoral hypercalcemia should be included in the differential diagnosis, particularly in patients with a past medical history of uterine leiomyoma, as such tumors may represent a potential source of PTHrP secretion.

In such cases, aggressive hydration and low-calcium dialysis have been shown to be effective in the management of hypercalcemia, thereby preventing maternal and fetal complications. Dialysis is an effective treatment option for the interim period until delivery. Definitive management consists of myomectomy and delivery, which also reduce estrogen levels.

Although the inability to measure PTHrP represents a significant limitation in the management of this case, the rapid normalization of calcium levels after delivery and myomectomy, along with the clinical course, strongly suggests that the hypercalcemia was PTHrP-mediated and originated from the

placenta or uterine leiomyoma.

Author contributions

We declare that all authors have accepted the submission and that the manuscript has not been published in whole or in part or submitted elsewher

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Tables

Table-1 Laboratory findings at admission

Parameter	Value	Reference Range
Complete Blood Count		
Hemoglobin(Hb)	10.3 gr/dl	12-16 gr/dl
WBCs	16.7x10.000 mcL	4.5-10 x10.000 mcL
Platelets	160.000/mcL	150-450.000/ mcL
Serum Biochemistry Results		
SerumCreatinine	0,59 mg/dl	0.5-0.9 mg/dl
Serum Na	136 mmol/l	135-145 mmol/l
Total Calcium	18.8 mg/dl	8.6-10.2 mg/dl
Ionized Calcium	2.17mmol/L	1.12-1.29 mmol/L
Serum Phosphorous	2.6 mg/dl	2.5-4.5 mg/dl.
ALT/AST	10/15 U/L	8-34/8-31U/L
Alkaline phosphatase	136 U/L	35-104 U/L
Albumin	32 g/L	35–52 g/L
Parathormone	4,4 mg/dl	16-38 mg/dl
TSH	0.86 mIU/l	0.45-4.5 mIU/l
25-OH-vitamin D 1.25 (OH) vitamin D	25 mcg/L 22 ng/L	30-180 mcg/L 18-78 ng/L

Table-2 Summary of the cases reported in the literature

	Case 1 (11)	Case 2 (6)	Case 3 (12)	Case 4 (13)	Case 5 (7)	Our Case
Maternal age	32	26	36	38	45	35
Gestational age	29 week	14 week	First month	31 week	31 week	37 week
Presentation	Lethargy, nausea and vomiting	Nausea and vomiting	Nausea and vomiting	Nausea and vomiting, Hypertension and acute pancreatitis	Dehydration with hypotension and tachycardia, delirium, and malnutrition	Itching, nausea and vomiting
Clinical progress	33 week, aspiration pneumonitis, vaginal delivery	D&C	34 week Emergency C/S	Emergency C/S	Emergency C/S	Emergency C/S
Max Ca level	20.8 mg/dl (8.8-11.2)	14.5 mg/dl (8.8-11.2)	19.2 mg/dl (8.8-11.2)	15,9 mg/dl (8.6-10.3)	17.92 mg/dL (8.8-11.2)	18,8 mg/dl (8.6 - 10.2)
Neonatal Period	IUGR	D&C	Not avaliable	No problem	Prematurity, temporary hypercalcemia	No problem
Surgery	Delivery+myo-mectomy	D&C-6 weeks later, surgery of fibroma	C/S-myo-mectomy	C/S-myomectomy	C/S- because of severe Hemorrhage without myomectomy	C/S-myomectomy
PTH level	Not avaliable	Not avaliable	0.3 pmol/L (1.6-6.9)	5 pg/ml (12-88)	<9,4 pg/nl (9.4-66.0)	4,4 ng/L (15-65)
PTHrP level	22 (<2)	46 (<15)	Not avaliable	9.6 (<4.2)	33 pmol/L < 3.4 pmol/L in pregnancy	Not avaliable
Treatment	Hydration, furosemid, pamidronat after delivery, dialysis	Hydration, furosemid, Cinacalcet, pamidronat	Hydration, Calcitonin, dialysis	Hydration, Calcitonin	Hydration, Calcitonin	Hydration, Dialysis
Histopathological Examination	23 cm diameter, benign, histological PTHrP staining (+)	Placenta PTHrP staining (+), fibroma staining (+)	23 cm diameter, benign, calcification (+)	19 cm diameter, benign		18 cm, benign

Figure 1 Mean serum calcium trend including 33rd week value

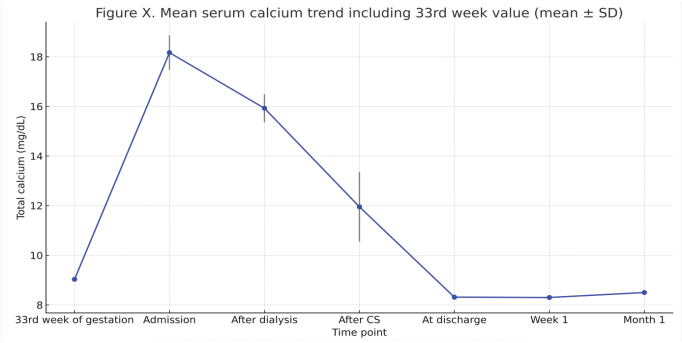

Figure 2 Microscopy of Myoma

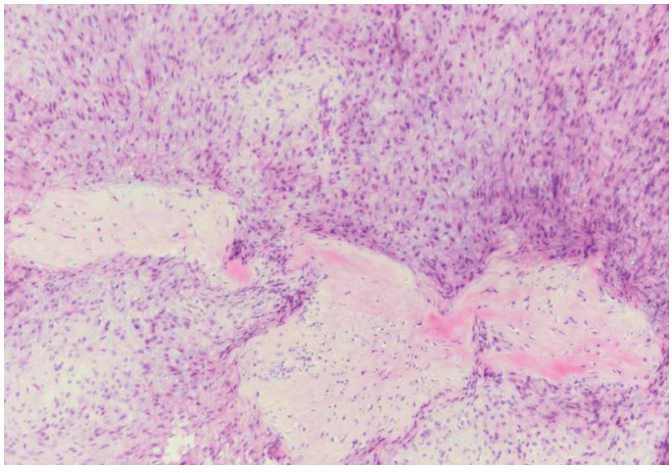

Figure 3-Macroscopy of of Myoma

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ACADEMIC JOURNAL OF HEALTH

CASE REPORT

Case Report Of Liver Neuroendocrine Tumor Detected Incidentally During Ovarian Cyst Surgery; Liver Neuroendocrine Tumor and Ovarian Cyst

ABSTRACT

Introduction: Neuroendocrine tumors, which are also known as carcinoid tumors (also "Argentaffin" or "Kulchitsky Cells"), are derived from embryonal neural crest cells that have the potential to regulate hormone secretion. The aim of this article is to present a liver neuroendocrine tumor that was detected incidentally in a patient who underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy due to an ovarian mass.

Case Report: A 73-year-old female patient applied with complaints of abdominal pain and swelling. A solid mass of 15 cm that originated from the right adnexal area was detected. During the surgery of this mass, the intra-abdominal evaluation revealed a nodular lesion in the liver incidentally. The final pathology result revealed an ovarian serous borderline tumor and liver neuroendocrine tumor.

Conclusion: During abdominal surgery, especially for mass surgery, manual exploration of the abdominal organs is very important even if not detected on preoperative imaging. Incidentally detected masses may be part of a syndrome or primary tumors. A differential diagnosis must also be made in terms of paraneoplastic syndrome.

Keywords: Neuroendocrine tumor, liver, adnexal mass, serous borderline

Introduction

Neuroendocrine tumors (NETs), also called carcinoid tumors (also called "Argentaffin" or "Kulchitsky cells"), derive from embryonal neural crest cells that may also have the potential to secrete hormones (1). It shows different clinical manifestations depending on its components and location (2). Recent epidemiologic analyses have indicated that neuroendocrine tumors (NETs) occur most frequently in the lung, with an incidence rate of 1.49 per 100,000 individuals, followed by 1.05 per 100,000 in the small intestine, 1.04 per 100,000 in the rectum, and 0.48 per 100,000 in the pancreas (3). However, the liver is a common site for metastatic NETs and neuroendocrine carcinomas (NECs), leading to difficulties in determining whether a neuroendocrine neoplasm in the liver is primary or metastatic (4).

It can be difficult to diagnose because of its nonspecific radiographic characteristics, often confused with other types of liver lesions. However, histopathology and immunohistochemistry may help to make the correct diagnosis of NETs (5).

Symptoms of undetected and untreated neuroendocrine tumors can be wide-ranging, such as uncontrolled hypertension, headache, facial flushing, sweating, flushing, heart rhythm disturbances, panic attack symptoms, and anxiety (6). They generally show a slow progression. Tumor burden might be asymptomatic or present quite severe clinical symptoms in proportion to the size of the mass. Classification is made according to the histological tumor grading (Table 1).

Its overall prognosis is better than other types of liver cancer with an average survival of 16.5 months (7). It may recur or metastasize within 1-10 years after surgical resection. The prognosis of primary hepatic NECs is extremely poor. The 5-year survival rate is only 5.8% and the 1-year survival rate is 23.5% for metastatic poorly differentiated NEC (7, 8).

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It is important to determine the diagnosis and differential diagnosis well. Symptoms may coexist in many ways. Chromogranin A, neurospecific enolase, pancreatic polypeptide, pancreastatin biomarkers can be used in diagnosis, treatment and monitoring (9).

The purpose of this case report was to present the coexistence of an independent liver NET and ovarian serous borderline tumor, which was operated in our clinic because of an adnexal mass and was not detected in preoperative imaging.

Case Report

The patient was 73 years old and presented to the clinic with complaints of abdominal pain and swelling. She had diabetes mellitus and coronary artery disease as comorbidities. Pelvic sonography revealed a thick-walled solid mass of approximately 15 cm in the right adnexal area with multiple nodularities. Preoperative tumor markers CA-125 (184 u/mL) and CA 19-9 (52.5 u/mL) were elevated. Contrast-enhanced magnetic resonance imaging of the whole abdomen revealed a cystic lesion in the right lower half of the abdomen (127x122x107 mm, hypointense on T1-weighted images, hyperintense on T2-weighted images, no contrast uptake after IVCM injection) and no pathologic findings were found in the liver. Hypointense nodular areas in the lesion wall on T2-weighted images were consistent with calcification.

The patient was taken into surgery after appropriate preoperative preparations. During abdominal observation, a 12x15 cm torsionized ecchymotic and necrotic cystic mass arising from the right ovary was detected. There were no findings suggestive of torsion in the preoperative imaging. The diagnosis was made intraoperatively. During surgery, all adnexal structures were found to be torsioned and adherent as a conglomerated mass. The torsiated mass was edematous and densely adherent to the proximal cecum and appendix. The mass was excised. During abdominal inspection, a nodular lesion was incidentally detected in the 6th segment of the liver. The hepatic mass was also excised for pathologic examination. The final pathology result revealed an ovarian serous borderline tumor and liver neuroendocrine tumor.

NET in the liver by Hematoxylin-Eosin (H&E) staining at 40x and 100x magnification is shown in figures 1 and 2. Postoperative PET CT results showed no other organ pathology, and the patient was followed up at short intervals. Patient management included postoperative check-ups on the 10th day, 1st month, and 3rd month.

Discussion

In this case report, we report a case of hepatic NET that was not detected on preoperative imaging but was detected on intraoperative inspection and palpation in a patient undergoing surgery for a possible gynecologic malignancy. This case demonstrates the importance of intraoperative inspection, even if preoperative imaging is negative.The most important point is to suspect criteria that may be symptoms of NET.Chronic hot flushes and/or diarrhea are typical symptoms of carcinoid syndrome caused by the release of serotonin and other vasoactive substances into the systemic circulation. Clinical signs such as hypertension, flushing, headache and excess serotonin may be indicative. Pain, gastrointestinal symptoms and fatigue are the most common initial symptoms (10,11). The rarity of PHNETs makes their diagnosis challenging. While imaging is not always significant, it clearly demonstrates the importance of exploration. The majority of liver NETs are metastases from the gastrointestinal tract or pancreas (10). Therefore, a comprehensive diagnostic approach with endoscopy, somatostatin receptor imaging, PETCT, and biochemical testing for activation biomarkers is necessary to exclude extrahepatic primary lesions. In our case, no extrahepatic primary focus was identified, confirming the diagnosis of a primary hepatic lesion. This approach is consistent with the recommendations of the North American Neuroendocrine Tumor Society (NANETS), which emphasizes systematic evaluation to determine tumor origin before definitive diagnosis and treatment.

The patient was diagnosed with acute hypertension during hospitalization, and vasomotor symptoms were not prominent. However, acute abdominal findings were the patient's most significant symptom.

In another clinical case with the same demographic characteristics as our case, liver metastases are frequently seen in NETs.Since Edmonson first reported primary hepatic neuroendocrine tumor (PHNET) in 1958, a total of 150 cases have been reported in the English literature and this number corresponds to approximately 0.3% of all NET cases (12). Carcinoid tumors most commonly metastasize to regional lymph nodes, liver, lung, bone and peritoneal cavity (12,13,14). Many patients present to the outpatient clinic with abdominal pain of unknown origin, fatigue, or incidental findings. In our patient, acute abdominal symptoms were the primary presenting symptoms; however, classic carcinoid findings, such as flushing, diarrhea, or bronchospasm, were absent. This clinical presentation can be explained by the literature, which indicates that hormonal symptoms are generally lacking in hepatic NETs due to the metabolism of vasoactive substances during the initial hepatic passage.

It is necessary to differentiate it from paraneoplastic syndromes or to determine the origin of this effect (15). Paraneoplastic syndromes are caused by factors such as adrenocorticotropic hormone and serotonin and vary depending on the biological activity of the tumor. Although the clinical findings are similar, the etiology is different (16). Endocrine and paraneoplastic findings can further complicate the clinical picture. Cases of paraneoplastic Cushing's syndrome due to ectopic adrenocorticotropic hormone (ACTH) secretion have been reported in gastrointestinal NETs (15). These syndromes can lead to severe metabolic and endocrine disorders that affect patient outcomes. Although these syndromes can mimic carcinoid features, their pathophysiologies are distinct and

require careful differentiation to guide appropriate treatment

The quality of life of cancer patients is affected not only by tumors and local malignancies but also by many symptoms. During abdominal surgeries, it is important to know the anatomy and to evaluate the adjacent organs in detail. Detection of incidental masses is an area that should be evaluated in case of detection of primary or metastatic lesions. Although imaging modalities can provide guidance, they should not be used alone.

Author contributions

We declare that all authors have accepted the submission and that the manuscript has not been published in whole or in part or submitted elsewhere.

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

Table and Figures

Table 1. Classification for Neuroendocrine Neoplasms

Well-differentiated NETs	Ki-67 Index (%)	Mitotic Index
Grade 1	<3	<2/10HPF
Grade 2	3–20	2–20/10HPF
Grade 3	>20	>20/10HPF
Poorly-differentiated NECs		
Grade 3 (Neuroendocrine Carcinoma)	>20	>20/10HPF

Figure 1: Pathological image of liver neuroendocrine tumor

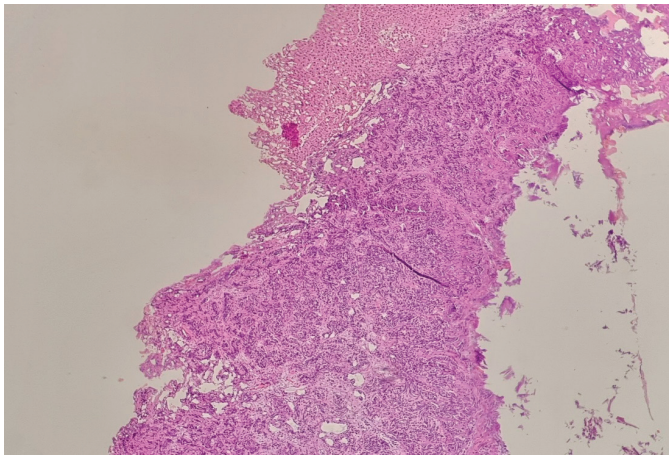

Figure 1 Liver Normal and Tumor Tissue H&E 40X

Figure 2: Neuroendocrine Tumor Cell

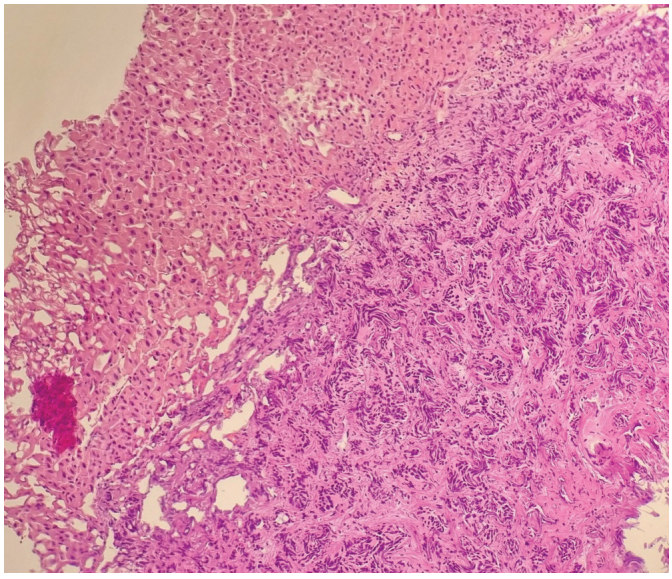

Figure 2 Islands consisting of oval and round cells and the trabeculae tumor with a crush artifact H&E 100X

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