Received: 08 July 2025 / Accepted: 28 October 2025 / Publishedonline: 30 December 2025

DOI10.34689/SH.2025.27.6.012

UDC616.8-089

FACTORS OF LIMITED DIAGNOSIS OF PHARAMACORESISTANT EPILEPSY

Akmaral Suleimenova[1], https://orcid.org/0009-0001-2587-9248
Nazira Bekenova[1], https://orcid.org/0000-0002-4094-0211
Tamara Vochshenkova[1], https://orcid.org/0000-0003-0935-6217
Balzhan Kassiyeva[1], https://orcid.org/0000-0002-8452-7146
Alisher Aitkaliyev[1], https://orcid.org/0009-0002-9624-2663
Tatiana Belikhina[1],https://orcid.org/0000-0002-1119-7457
ZhassulanUtebekov[1], https://orcid.org/0009-0006-6272-5033
Mukhit Dossov[1], https://orcid.org/0009-0000-3291-362X

[1]Medical Center Hospital of the President,s affairs Administration of the Republic of Kazakhstan, Astana, the Republic of Kazakhstan.

Abstract

Background: Drug-resistant epilepsy (DRE) remains a serious clinical challenge, especially in settings with limited access to specialized care. A significant proportion of patients in Kazakhstan do not receive timely diagnosis or referral to specialized centers.

Objective: The aim of this study is to identify, using the example of the Epilepsy center's work, the barriers that limit access to specialized treatment, particularly the timely establishment of a diagnosis of drug-resistant epilepsy.

Materials and methods: This retrospective observational study included 560 Kazakh patients with DRE who presented to the Center between 2017 and 2023. Clinical and demographic data, social status, place of residence, and access to specialized care were analyzed. Statistical processing was performed using non-parametric methods and the χ^2 test, with a significance level of $p < 0.05$.

Results: In the overall patient group, delayed identification of drug resistance was associated with marital status and region of residence. Among patients whose diagnosis was first established at the Epilepsy center, unmarried individuals predominated ($p < 0.006$). A statistically significant predominance of individuals from Astana who received specialized care was observed ($p < 0.0001$). Examination of the association between DRE diagnosis and different epilepsy duration groups revealed no significant relationship in any group. Analysis of factors contributing to delayed DRE diagnosis in patients with disease duration over 20 years showed that men were almost 1.5 times more likely to experience delayed diagnosis compared to women (OR, 95% CI: 1.12 (1.02–1.31), $p = 0.02$), and lack of social protection reduced the likelihood of receiving specialized care (OR, 95% CI: 0.65 (0.54–0.79), $p < 0.0001$).

Conclusions: Timeliness of DRE diagnosis in Kazakhstan is determined by a combination of sociodemographic and regional factors. Patients from Astana and those with social support have better access to specialized care. Systemic measures are needed to improve patient referral pathways, reduce regional disparities, and combat stigmatization.

Keywords: *drug-resistant epilepsy, epilepsy duration, delayed diagnosis, specialized care.*

For citation:

Suleimenova A., Bekenova N., Vochshenkova T., Kassiyeva B., Aitkaliyev A., Belikhina T., Utebekov Zh., Dossov M., Factors of limited diagnosis of pharamacoresistant epilepsy // Nauka i Zdravookhranenie [Science & Healthcare]. 2025. Vol.27 (6), pp. 101-108. doi 10.34689/SH.2025.27.6.012

Резюме

ФАКТОРЫ ОГРАНИЧЕННОЙ ДИАГНОСТИКИ ФАРМАКОРЕЗИСТЕНТНОЙ ЭПИЛЕПСИИ

Акмарал Сулейменова[1], https://orcid.org/0009-0001-2587-9248
Назира Бекенова[1], https://orcid.org/0000-0002-4094-0211
Тамара Вощенкова[1], https://orcid.org/0000-0003-0935-6217
Балжан Касиева[1], https://orcid.org/0000-0002-8452-7146
Алишер Айткалиев[1], https://orcid.org/0009-0002-9624-2663
Татьяна Белихина[1], https://orcid.org/0000-0002-1119-7457

Жасулан Утебеков[1], https://orcid.org/0009-0006-6272-5033
Мухит Досов[1], https://orcid.org/0009-0000-3291-362X

[1]Больница Медицинского центра Управления делами Президента Республики Казахстан, г. Астана, Республика Казахстан.

Введение. Фармакорезистентная эпилепсия (ФРЭ) остаётся серьёзной клинической проблемой, особенно в условиях ограниченного доступа к специализированной помощи. Значительная часть пациентов в Казахстане не получает своевременную диагностику и направление в специализированные центры.

Целью данного исследования является на примере работы Центра выявить барьеры, ограничивающие доступ к специализированному лечению, в частности своевременное установление диагноза фармакорезистентной эпилепсии.

Материалы и методы. Ретроспективное наблюдательное исследование включало 560 пациентов казахской национальности с ФРЭ, обратившихся в Центр с 2017 по 2023 гг. Анализировались клинико-демографические данные, социальный статус, место проживания и доступ к специализированной помощи. Статистическая обработка данных проводилась с использованием непараметрических методов и χ^2-теста, уровень значимости $p < 0,05$.

Результаты. В общей группе пациентов с несвоевременным выявлением фармакорезистентности были связаны семейное положение и регион проживания пациента. Среди пациентов, у которых диагноз впервые установлен в Центре эпилепсии, преобладали неженатые/незамужние ($p<0,006$). Наблюдается статистически значимое преобладание лиц в Астане, получивших специализированную помощь ($p<0,0001$). Изучение ассоциации с диагнозом фармакорезистентности в разных группах в зависимости от продолжительности эпилепсии не показала значимой связи ни в одной из групп. Анализ факторов несвоевременной постановки диагноза фармакорезистентности в группе пациентов с длительностью заболевания более 20 лет показал, что среди мужчин почти в 1,5 раза была вероятность несвоевременного диагностирования по сравнению с женщинами (OR, 95% CI: 1,12 (1,02-1,31), p=0,02) и отсутствие социальной защиты уменьшает шансы на получение специализированной помощи (OR, 95% CI: 0,65 (0,54-0,79), p<0,0001).

Выводы. Своевременность диагностики ФРЭ в Казахстане определяется сочетанием социально-демографических и региональных факторов. Пациенты из Астаны и социально защищённые лица обладают более высокой доступностью специализированной помощи. Необходимы системные меры по улучшению маршрутизации пациентов, снижению регионального неравенства и борьбе со стигматизацией.

Ключевые слова: *фармакорезистентная эпилепсия, длительность эпилепсии, несвоевременная диагностика, специализированная помощь.*

Для цитирования:

Сулейменова А., Бекенова Н., Вощенкова Т., Касиева Б., Айткалиев А., Белихина Т., Утебеков Ж., Досов М. Факторы ограниченной диагностики фармакорезистентной эпилепсии // Наука и Здравоохранение. 2025. Vol.27 (6), С. 101-108. *doi 10.34689/SH.2025.27.6.012*

Түйіндеме

ФАРМАКОРЕЗИСТЕНТТІ ЭПИЛЕПСИЯНЫҢШЕКТЕУЛІДИАГНОСТИКАЛЫҚФАКТОРЛАРЫ

Акмарал Сулейменова[1], https://orcid.org/0009-0001-2587-9248
Назира Бекенова[1], https://orcid.org/0000-0002-4094-0211
Тамара Вощенкова[1], https://orcid.org/0000-0003-0935-6217
Балжан Касиева[1], https://orcid.org/0000-0002-8452-7146
Алишер Айткалиев[1], https://orcid.org/0009-0002-9624-2663
Татьяна Белихина[1], https://orcid.org/0000-0002-1119-7457
Жасулан Утебеков[1], https://orcid.org/0009-0006-6272-5033
Мухит Досов[1], https://orcid.org/0009-0000-3291-362X

[1]Қазақстан Республикасы Президенті Іс Басқармасының Медициналық орталығының ауруханасы, Астана қ., Қазақстан Республикасы.

Кіріспе. Фармакорезистентті эпилепсия (ФРЭ), әсіресе мамандандырылған көмекке қол жетімділік шектеулі жағдайларда, маңызды клиникалық мәселе болып қала береді. Қазақстандағы пациенттердің едәуір бөлігі уақтылы диагноз қойып, мамандандырылған орталықтарға жолдама алмайды.

Мақсат. Бұл зерттеудің мақсаты орталық жұмысының мысалында мамандандырылған емдеуге қол жеткізуді шектейтін кедергілерді анықтау, атап айтқанда фармакорезистентті эпилепсия диагнозын уақтылы анықтау болып табылады.

Материалдар мен әдістер. Ретроспективті байқау зерттеуі 2017 жылдан 2023 жылға дейін Орталыққа жүгінген ФРЭ бар қазақ ұлтының 560 пациентін қамтыды. Статистикалық деректерді өңдеу параметрлік емес әдістер мен сынақтың көмегімен жүргізілді σ2, маңыздылық деңгейі p < 0,05.

Нәтижелер. Фармакорезистенттілігі уақтылы белгіленбеген пациенттердің жалпы тобында пациенттің отбасылық жағдайы мен тұратын аймағы байланысты болды. Эпилепсия орталығында алғаш диагноз қойылған пациенттер арасында үйленбеген / үйленбеген адамдар басым болды (p<0,006). Астанада мамандандырылған көмек алған адамдардың статистикалық маңызды артықшылығы байқалады (p<0,0001). Эпилепсияның ұзақтығына байланысты әртүрлі топтардағы фармакорезистенттілік диагнозымен байланысты зерттеу екі топта да айтарлықтай байланыс таппады. Аурудың ұзақтығы 20 жылдан асатын пациенттер тобындағы фармакорезистенттілік диагностикасының уақтылы емес факторларын талдау ер адамның уақтылы диагноз қою ықтималдығы әйелдерге қарағанда шамамен 1,5 есе жоғары екенін көрсетті (OR, 95% ci: 1,12 (1,02-1,31), p=0,02), ал әлеуметтік қорғаудың болмауы мамандандырылған көмек алу ықтималдығын төмендетеді (OR, 95% ci: 0,65 (0,54-0,79), p<0,0001).

Қорытынды. Қазақстанда ФРЭ диагностикасының уақтылығы әлеуметтік-демографиялық және өңірлік факторлардың үйлесімімен айқындалады. Астанадан келген пациенттер мен әлеуметтік қорғалған адамдар мамандандырылған көмектің жоғары қолжетімділігіне ие. Пациенттердің маршруттауын жақсарту, аймақтық теңсіздікті азайту және стигматизациямен күресу үшін жүйелі шаралар қажет.

Түйінді сөздер: *фармакорезистентті эпилепсия, эпилепсияның ұзақтығы, уақтылы диагностика, мамандандырылған көмек.*

Дәйексөз үшін:

Сулейменова А., Бекенова Н., Вощенкова Т., Касиева Б., Айткалиев А., Белихина Т., Утебеков Ж., Досов М. Фармакорезистентті эпилепсияның шектеулі диагностикалық факторлары // ғылым және Денсаулық сақтау. 2025. Vol.27 (6), Б. 101-108. doi 10.34689/SH.2025.27.6.012

Introduction

Epilepsy is one of the most prevalent neurological disorders, particularly in low- and middle-income countries [5]. In most cases (approximately 60–70%), seizures can be successfully controlled with antiseizure medication; however, in about one third of patients, pharmacoresistant epilepsy (PRE) develops a condition in which seizures persist despite adequate pharmacological therapy [12].

Pharmacoresistant epilepsy is defined as the failure to achieve complete or near-complete seizure control despite the use of two “appropriate” antiepileptic drug (AED) regimens, administered either as monotherapy or in combination. The prevalence of PRE ranges from 15% in children to up to 34% in adults [4, 14, 17]. This condition leads to severe consequences, including psychosocial dysfunction, reduced quality of life, increased risk of injury, and premature mortality. Patients often become preoccupied with their condition, experience a significant decline in quality of life, and develop psychiatric comorbidities such as depression and anxiety. In addition, academic performance may deteriorate, social interactions become restricted, and in some cases, complete social isolation may occur [2,18].

Particular attention in clinical practice and research is given to focal epilepsy, in which the issue of pharmacoresistance is especially critical. In cases with confirmed structural abnormalities and well-localized epileptogenic foci, surgical intervention may represent a radical and effective treatment option [7]. As emphasized in clinical guidelines, for pharmacoresistant focal epilepsy, surgical treatment often has advantages over continued pharmacological therapy alone [8].

Nevertheless, despite clear indications and proven efficacy, epilepsy surgery remains insufficiently implemented in several Central Asian countries, including Kazakhstan. The most commonly identified barriers include diagnostic, infrastructural, socioeconomic, and organizational factors that hinder timely access to specialized care for patients with PRE [9, 15]. A particularly important issue is limited diagnostic capacity: decision-making regarding surgery requires high-quality neuroimaging (high-field MRI), video-EEG monitoring, and often invasive electrocorticography. In settings with limited resources and restricted availability of these modalities, significant obstacles arise that impede appropriate selection of surgical candidates. Collectively, these factors exacerbate the problem, as patients with pharmacoresistant focal epilepsy fail to receive timely surgical treatment, adversely affecting their quality of life as well as their cognitive and social functioning.

It is well established that specialized epilepsy care is provided through dedicated epilepsy centers. In Kazakhstan, three epilepsy centers are currently operating, with the primary aim of delivering comprehensive diagnostic and therapeutic services for patients with epilepsy. All preoperative and postoperative procedures are covered by the patient, whereas the surgical intervention itself is funded by the state. The Epilepsy Center of the Medical Center Hospital of the President’s Affairs Administration of the Republic of Kazakhstan (hereinafter referred to as the Center) began its operations in 2018 and is based on interdisciplinary collaboration among specialists from various fields, including epileptologists, neurosurgeons, experts in neurophysiology and neuroimaging, and pathologists. Despite these developments, recently published data indicate that only approximately 25–30% of patients with pharmacoresistant epilepsy in Kazakhstan have access to surgical treatment [1]. Consequently, only a limited proportion of patients with epilepsy receive specialized care at such centers, and the diagnosis of pharmacoresistant epilepsy may remain unrecognized for a prolonged period.

The aim of this study is to identify, using the experience of a Center as an example, the barriers that limit access to specialized care, with particular emphasis on the timely diagnosis of pharmacoresistant epilepsy.

Materials and Methods

This retrospective observational study included 560 patients with pharmacoresistant epilepsy who were referred to the Epilepsy Center of the Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan between early 2017 and late 2023. Patients were divided into two groups: those in whom pharmacoresistance was first diagnosed at the Center (n = 467) and those with previously established pharmacoresistant epilepsy (n = 93). All study participants were of Kazakh ethnicity. A retrospective analysis of clinical and anamnestic data was performed. Clinical information was obtained from the epilepsy surgery database and through review of hospital medical records. To ensure data specificity and accuracy, all records were additionally verified through manual review for consistency with the diagnosis as well as inclusion and exclusion criteria.

Individual participant data included date of birth, sex, ethnicity, age at epilepsy onset, age at obtaining the Center's diagnostic conclusion, age at initiation of antiseizure medication (ASM) therapy, duration and status of epilepsy and pharmacoresistance, and, in cases of surgical treatment, age at the time of surgery. In addition, information on patients' social status, place of residence, and distance from the Center was collected.

Regions of residence were categorized into four groups based on their distance from the Center: Group 1 - Astana; Group 2 - outside Astana up to 500 km; Group 3 - outside Astana at a distance of 500–999 km; and Group 4 - outside Astana 1,000 km or more. However, for analytical purposes, place of residence was ultimately dichotomized into Astana versus other regions.

Inclusion criteria were as follows: age ≥18 years at the time of referral to the Center; pharmacoresistant epilepsy (failure of ≥2 adequately tried and tolerated antiseizure medications); diagnosis consistent with the International League Against Epilepsy (ILAE) criteria for pharmacoresistant epilepsy; and Kazakh ethnicity.

Exclusion criteria included the presence of malignancy, any chronic disease in a decompensated stage, non-focal forms of epilepsy, and incomplete medical records.

Pharmacoresistant epilepsy (PRE) was defined as the failure to achieve sustained seizure remission despite treatment with two well-tolerated, appropriately selected, and adequately dosed antiepileptic drugs, administered either as monotherapy or in combination. In this context, the results of therapeutic drug monitoring of valproic acid and carbamazepine (Finlepsin), available at the Center, were evaluated.

*Ethical Considerations.*This study was conducted in accordance with an extended protocol for the secondary analysis of anonymized medical data and received ethical approval from the Local Bioethics Committee of the hospital, as stated in Protocol No. 4 dated December 20, 2024, and in compliance with the Declaration of Helsinki.

*Statistical Analysis.*Statistical analysis was performed using SPSS (IBM) version 26.0. Quantitative data were analyzed as continuous variables and presented as medians with lower and upper quartiles, Me (Q1; Q3), as well as means with standard deviations (M ± SD), where appropriate. Qualitative data were presented as frequencies and proportions and were dichotomized for analysis.

Quantitative data with non-normal distribution were analyzed using the nonparametric Mann–Whitney U test for independent groups, with results reported as medians (Q1; Q3). Data normality was assessed using the Shapiro–Wilk test. Dichotomous and categorical variables were analyzed using the chi-square (χ^2) test. A p-value of <0.05 was considered statistically significant. Associations between factors and pharmacoresistance were assessed using Pearson's chi-square (χ^2) test and odds ratios (ORs) with 95% confidence intervals (CIs).

Results

The results of our study demonstrated that the mean age at which pharmacoresistant epilepsy was first identified at the Center was significantly younger than that of patients with previously established pharmacoresistance. The age at seizure onset among patients with newly diagnosed pharmacoresistant epilepsy was younger than in those with a previously established diagnosis; however, these differences did not reach statistical significance. The duration of epilepsy was significantly longer in the group with a previously established diagnosis compared to patients in whom pharmacoresistance was first identified at the Center.

The proportion of male patients was higher in the group with a previously known diagnosis of pharmacoresistant epilepsy. In contrast, women slightly predominated among patients with newly diagnosed pharmacoresistance; however, no statistically significant association between sex and the timing of pharmacoresistant epilepsy diagnosis was observed.

Marital status, however, was associated with delayed diagnosis. Among patients whose diagnosis of pharmacoresistant epilepsy was first established at the Center, the proportion of unmarried individuals was higher than that of married patients.

Place of residence was not associated with the timeliness of diagnosis. In both the newly diagnosed and previously known pharmacoresistant epilepsy groups, urban residents predominated.

In both groups, the majority of patients were unemployed or not formally organized in the workforce. The proportion of socially unprotected patients exceeded that of socially protected individuals in both groups; however, no statistically significant differences between the groups were identified.

Our findings also indicated that, compared with the city of Astana, the number of patients with timely diagnosis in other regions was substantially lower. These differences were statistically significant and reflect a predominance of individuals in Astana who received specialized medical care.

Regarding the overall duration of epilepsy, both in the group with newly diagnosed pharmacoresistant epilepsy at the Epilepsy Center and in the group with a previously established diagnosis of pharmacoresistant epilepsy, the duration of the disease exceeded 20 years. However, in the group with a previously known diagnosis of pharmacoresistant epilepsy, the disease duration was statistically significantly longer than in the group with a newly established diagnosis.

As shown in Table 1, the proportion of patients with an epilepsy duration of up to 5 years was higher among those with

previously established pharmacoresistant epilepsy, whereas a disease duration of 5 to 10 years was more frequently observed among patients in whom pharmacoresistance was first identified at the Center. Patients with an epilepsy duration of 10 to 20 years were more common in the group with previously known pharmacoresistance. The largest proportion of patients belonged to the group with a disease duration exceeding 20 years. In this category, the proportion of patients was equal in both groups - those with newly identified pharmacoresistance and those with previously established pharmacoresistance.

However, no statistically significant association between the timeliness of pharmacoresistance detection and epilepsy duration was identified in either group. Although certain trends were observed when comparing the 5–10-year and 10–20-year subgroups, these associations did not reach statistical significance due to the application of Bonferroni correction for six pairwise comparisons.

Table 1.

Clinical and Demographic Indicators and Comparative Characteristics Based on the Detection of Pharmacoresistance.

Indicators	Newly Diagnosed Pharmacoresistance	Previously Known Pharmacoresistance	p
Gender	467	93	
Male	233(49,9%)	53(56,9%)	0,21
Female	234(50,1%)	40(43,1%)	
Marital Status	467	93	
Married	213(45,6%)	57(61,3%)	<0,006
Unmarried	254(54,4%)	36(38,7%)	
Average age, years	36,0 (31,0-41,0)	39,0(41,0-56,0)	<0,0001
Age at seizure onset, years	13,0(7,0-19,0)	21,0(13,0-33,0)	0,31
Duration of epilepsy, years	23,0(16,0-29,0)	27,0(16,0-32,5)	0,009
Place of residence	467	93	
City	371 (79,4%)	81 (87,1%)	0,09
Village	96 (20,6%)	12 (12,9%)	
Employment status	467	93	
Employed	156 (33,4%)	31 (33,3%)	0,99
Unemployed	311 (66,6%)	62 (66,7%)	
Social support	467	93	
Has group	189 (40,5%)	40 (43,1%)	0,65
No group	278 (59,5%)	53 (56,9%)	
Region	467	93	
Astana	213 (45,6%)	66 (70,9%)	<0,0001
Other regions	254 (54,4%)	27 (29,1%)	

Table 2.

Distribution of Patients by Epilepsy Duration and Comparison of Risk Indicators (Odds Ratio, OR) for Newly Diagnosed and Previously Established Pharmacoresistance.

Duration of epilepsy	Newly DiagnosedPR (n=467)	Previously Established PR (n=93)	OR (95% CI)	p
Upto 5 years	32 (6.85%)	7 (7.53%)	3,28 (0,63-17,1)	0,14
From 5 to 10 years	28 (6.0%)	1 (1.1%)		
From 5 to 10 years	28(6.0%)	1(1.1%)	1,25 (1,09-1,44)	0,05
From 10 to 20 years	89 (19.1%)	20 (21.5%)		
From 10 to 20 years	89(19.1%)	20(21.5%)	1,07 (0,61-1,88)	0,82
Over 20 years	318 (68.1%)	65 (69.9%)		
Upto 5 years	32(6.85%)	7(7.53%)	1,00 (0,39-2,61)	0,99
From 10 to 20 years	89(19.1%)	20(21.5%)		
From 5 to 10 years	28(6.0%)	1(1.1%)	0,33 (0,08-1,40)	0,11
Over 20 years	318 (91,9%)	65 (98,5%)		
Upto 5 years	32 (6.85%)	7 (7.53%)	1,07 (0,45-2,53)	0,88
Over 20 years	318 (68.1%)	65 (69.9%)		

Given that the largest number of patients was observed in the group with an epilepsy duration exceeding 20 years, we further analyzed factors associated with delayed diagnosis of

pharmacoresistant epilepsy within this subgroup. The analysis demonstrated that sex and social protection status were statistically significant factors associated with prolonged non-detection of pharmacoresistance. Male patients had approximately a 1.5-fold higher likelihood of delayed diagnosis of pharmacoresistant epilepsy compared with female patients. Lack of social protection reduced the likelihood of receiving specialized care and timely diagnosis.

Other factors, including marital status, place of residence (urban vs. rural), employment status (employed vs. unemployed), and region, were not associated with the timeliness of diagnosis among patients with long-standing disease. Although a tendency toward a higher number of undiagnosed cases was observed in regions geographically distant from Astana, these differences did not reach statistical significance. The detailed data are presented in Table 3.

Table 3.

Factors Associated with Prolonged Epilepsy: A Comparative Analysis.

Factors	Disease duration over 20 years	Disease duration up to 20 years	OR (95% CI)	p
Gender	n=318	n=149	1,12 (1,02-1,31)	0,02
Male	171 (53,8%)	63 (42,3%)		
Female	147 (46,2%)	86 (57,7%)		
Marital Status				
Married	168 (52,8%)	86 (57,7%)	1,15 (0,88-1,50)	0,32
Unmarried	150 (47,2%)	63 (42,3%)		
Place of residence				
City	247 (77,7%)	124 (83,2%)	1,27 (0,88-1,83)	0,19
Village	70 (22,3%)	25 (16,8%)		
Employment status				
Employed	100 (31,5%)	55 (36,9%)	1,18 (0,89-1,55)	0,24
Unemployed	218 (38,5%)	94 (63,1%)		
Social support				
Has group	258 (81,1%)	88 (59,1%)	0,65 (0,54-0,79)	<0,0001
No group	60 (18,9%)	61 (40,9%)		
Region				
Astana	139 (43,7%)	75 (50,3%)	1,31 (0,88-1,93)	0,18
Other regions	179 (56,3%)	74 (49,7%)		

Discussion

The present study identified several sociodemographic and geographic factors that limit access to specialized care and contribute to delayed diagnosis of pharmacoresistant epilepsy (PRE). The proportion of delayed PRE diagnosis was higher among unmarried individuals and among patients residing in regions geographically distant from Astana. Moreover, we observed a proportional increase in the number of patients with longer disease duration, with more than half of newly diagnosed PRE cases being identified only after 20 years of disease progression. Among patients with an epilepsy duration exceeding 20 years, male sex and lack of social protection were significant factors associated with delayed diagnosis.

Although patients with newly diagnosed PRE in our cohort were younger and differed in disease duration compared with those with previously established pharmacoresistance, they nevertheless had a substantial duration of epilepsy (median 23 years). These findings highlight the issue of late recognition of PRE and are consistent with data from previous studies. It is well documented that, on average, patients wait 15–20 years from seizure onset before being referred for specialized diagnostic evaluation or surgical treatment, which substantially exceeds the recommended threshold of two years of treatment failure with two appropriately selected antiseizure medications, as defined by the International League Against Epilepsy (ILAE) [10].

We identified an association between marital status and the likelihood of timely diagnosis, with unmarried patients being more prevalent among those whose PRE was first diagnosed exclusively at the Center. According to international studies, having a partner is associated with better treatment adherence and more regular follow-up visits among patients with epilepsy [13]. However, within our sociocultural context, this finding may also be explained by disease-related stigma. Epilepsy remains one of the most highly stigmatized neurological disorders, and patients often conceal their diagnosis due to fear of discrimination and anxiety related to the unpredictable occurrence of seizures [6,16].

A statistically significant predominance of timely diagnosed cases was observed in Astana compared with other regions of Kazakhstan. Geographic disparities in access to specialized epileptological care have also been reported in other countries. Several studies indicate that patients living far from specialized epilepsy centers have significantly lower chances of receiving timely diagnosis and referral for epilepsy surgery [19]. Therefore, the regional differences observed in our study are not unique to Kazakhstan and likely reflect broader structural barriers within healthcare systems.

Despite the high proportion of patients with an epilepsy duration exceeding 20 years, no statistically significant association was found between disease duration and the timeliness of PRE diagnosis across epilepsy duration

subgroups. Nevertheless, the observed trends—such as more frequent delayed diagnosis among patients with disease duration of 10–20 years—warrant further investigation in a larger cohort. The predominance of disease duration exceeding 20 years in more than half of patients whose PRE was first diagnosed at the Center is particularly concerning and should alert clinicians to the risk of prolonged under-recognition of pharmacoresistance.

Despite the absence of an overall association between sex and the detection of pharmacoresistant epilepsy (PRE) in the entire cohort, male patients in the subgroup with long-standing disease duration (>20 years) were nearly 1.5 times more likely to experience delayed diagnosis of PRE. Recent meta-analytic evidence indicates no overall differences between men and women in access to specialized epilepsy care [11]. The sex-related effect on the timeliness of PRE diagnosis observed in our study among patients with disease duration exceeding 20 years may therefore reflect specific social and cultural characteristics of our country.

With regard to the impact of social support on the timeliness of PRE diagnosis in patients with long-standing epilepsy (>20 years), available literature indicates that individuals with lower socioeconomic status receive specialized care significantly less frequently [3], and low socioeconomic status is associated with a longer duration of uncontrolled seizures [20].

Conclusion

This study revealed pronounced social and regional disparities in the timeliness of pharmacoresistant epilepsy diagnosis and access to surgical treatment in Kazakhstan. Socially protected patients and residents of Astana demonstrated significantly higher likelihood of receiving specialized care. These findings highlight the need for comprehensive healthcare system interventions aimed at reducing social inequality, improving patient referral pathways through optimization of primary care practices, and eliminating regional barriers by enhancing communication systems and implementing health information technologies. In addition, educational and awareness-raising initiatives are required to address epilepsy-related stigma.

Funding

This study was conducted within the framework of the scientific and technical program BR28512409, "Development of a comprehensive innovative technology for diagnostic selection and surgical treatment of focal epilepsy resistant to drug therapy", funded by the Ministry of Science and Higher Education of the Republic of Kazakhstan.

Author Contributions

Conceptualization: A.S., N.B.;
Methodology: A.S., N.B., A.A., Zh.U.;
Investigation: N.B., A.S., T.A., M.A., Zh.U.;T.I.
Original draft preparation: A.S., N.B., Zh.U.;
Review and editing: N.B., B.K., A.A., T.A., Zh.U.

Literature:

1. *Akhmedullin R., Kozhobekova B., Gusmanov A., Aimyshev T., Utebekov Z., Kyrgyzbay G., Gaipov A.* Epilepsy trends in Kazakhstan: A retrospective longitudinal study using data from unified national electronic health system 2014–2020. Seizure: European Journal of Epilepsy. 2024. 122, 58-63. doi: 10.1016/j.seizure.2024.09.022

2. *Bauer P.R., Bronnec M.L., Schulze-Bonhage A., Altenmüller D.M., Fuchs T.* Seizures as a struggle between life and death: an existential approach to the psychosocial impact of seizures in candidates for epilepsy surgery. Psychopathology. 2023. 56(6), 417-429. doi: 10.1159/000528924

3. *Bernstein J., Kashyap S., Kortz M. W., ZakharyB., Takayanagi A., Toor H., Miulli D.* Utilization of epilepsy surgery in the United States: a study of the National Inpatient Sample investigating the roles of race, socioeconomic status, and insurance. Surgical Neurology International. 2021. 12, 546. doi: 10.25259/SNI_824_2021

4. *Denton A., Thorpe L., Carter A., Angarita-Fonseca A., Waterhouse K., Hernandez Ronquillo L.* Definitions and risk factors for drug-resistant epilepsy in an adult cohort. Frontiers in Neurology. 2021. 12, 777888. doi: 10.3389/fneur.2021.777888

5. *Espinosa-Jovel C., Toledano R., Aledo-Serrano Á., García-Morales I., Gil-Nagel A.* Epidemiological profile of epilepsy in low income populations. Seizure. 2018. 56, 67-72. doi: 10.1016/j.seizure.2018.02.002

6. *Esilva M.H., Lima J.V., da Silva Lopes I.P., da Silva A.C., Lucchi I.M., Oliveira G.P., Resende E.F.* Stigmas in Epilepsy: Systematic Review and Meta-Analysis. Journal of Epilepsy Research. 2025. 15(1), 23. doi: 10.14581/jer.25003

7. *Guery D., Rheims S.* Clinical management of drug resistant epilepsy: a review on current strategies. Neuropsychiatric disease and treatment. 2021. C. 2229-2242. doi: 10.2147/NDT.S256699

8. *Jobst B.C., Cascino G.D.*Resective epilepsy surgery for drug-resistant focal epilepsy: a review. Jama. 2015. 313(3), 285-293. doi: 10.1001/jama.2014.17426

9. *Kalinina D., Bekenova N., Muxunov A., Utebekov Z., Kyrgyzbay G., Kimadiev D., Sarria-Santamera A.* Epilepsy Surgery in Kazakhstan: Outcomes and the Role of Advanced Imaging. Journal of Clinical Medicine. 2025. 14(22), 7932. doi.org/10.3390/jcm14227932

10. *Kwan P., Brodie M.J.* Epilepsy after the first drug fails: substitution or add-on? Seizure. 2000. 9(7), 464-468. doi:10.1053/seiz.2000.0442

11. *Karakas C., Alam M. C., Ferreira L. D., Nair S., Kovalev D., Haneef Z.*Sociodemographic barriers in epilepsy surgery in the United States: A systematic review and meta-analysis. Epilepsy & Behavior. 2025. 167, 110391. doi: 10.1016/j.yebeh.2025.110391

12. *Löscher W., Potschka H., Sisodiya S. M., Vezzani A.* Drug resistance in epilepsy: clinical impact, potential mechanisms, and new innovative treatment options. Pharmacological reviews. 2020. 72(3), 606-638. doi: 10.1124/pr.120.019539

13. *Loring D.W., Lowenstein D.H., Barbaro N.M., Fureman B.E., Odenkirchen J., Jacobs M. P., Stout A.* Common data elements in epilepsy research: development and implementation of the NINDS epilepsy CDE project. Epilepsia. 2011. 52(6), 1186-1191. doi: 10.1111/j.1528-1167.2011.03018.x

14. *Marouf H., Mohamed L. A., El Ftatary A., Gaber D. E.* Prevalence and risk factors associated with drug-resistant epilepsy in adult epileptic patients. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2023. 59(1), 153.

15. *Menlibayeva K., Nurimanov C., Mammadinova I., Turzhanova A., Akshulakov S., Makhambetov Y.* Challenges in

the Management of Cavernoma-Related Epilepsy: Seizure Outcomes, Antiseizure Medication Practices, and Access to Intraoperative Technologies in Kazakhstan. Brain Sciences. 2025. 15(9), 992. doi.org/10.3390/brainsci15090992

16. *Mayor R., Gunn S., Reuber M., Simpson J.* Experiences of stigma in people with epilepsy: A meta-synthesis of qualitative evidence. Seizure. 2022. 94, 142-160. doi: 10.1016/j.seizure.2021.11.021

17. *Ramos-Lizana J., Rodriguez-Lucenilla M. I., Aguilera-Lopez P., Aguirre-Rodríguez J., Cassinello-García E.* A study of drug-resistant childhood epilepsy testing the new ILAE criteria. Seizure. 2012. 21(4), 266-272. doi: 10.1016/j.seizure.2012.01.009

18. *Ridsdale L., Wojewodka G., Robinson E., Landau S., Noble A., Taylor S., Goldstein L.H.* Characteristics associated with quality of life among people with drug-resistant epilepsy. Journal of neurology. 2017. 264(6), 1174-1184. doi: 10.1007/s00415-017-8512-1

19. *Soto V.E., Farfan M.I., Lorant V.* Fiscal decentralisation and infant mortality rate: The Colombian case. Social Science & Medicine. 2012. 74(9), 1426-1434. doi: 10.1016/j.socscimed.2011.12.051

20. *Szaflarski M.* Social determinants of health in epilepsy. Epilepsy & Behavior. 2014. 41, 283-289. doi: 10.1016/j.yebeh.2014.06.013

Author Information

Akmaral Suleimenova - MMS, Department of Science, Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan, 80 Mangilik El Avenue, Astana, Kazakhstan, https://orcid.org/0009-0001-2587-9248

Nazira Bekenova - MD, PhD, Department of Science, Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan, 80 Mangilik El Avenue, Astana, Kazakhstan,https://orcid.org/0000-0002-4094-0211

Tamara Voshchenkova - MD, MBA, Department of Science, Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan, 80 Mangilik El Avenue, Astana, Kazakhstan, https://orcid.org/0000-0003-0935-6217

Balzhan Kassiyeva - MMS, Department of Science, Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan, 80 Mangilik El Avenue, Astana, Kazakhstan, https://orcid.org/0000-0002-8452-7146

Alisher Aitkaliyev - MBiotech, Department of Science, Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan, 80 Mangilik El Avenue, Astana, Kazakhstan,https://orcid.org/0009-0002-9624-2663

Tatyana Belikhina - MD, Department of Science, Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan, 80 Mangilik El Avenue, Astana, Kazakhstan, https://orcid.org/0001-0002

Zhassulan Utebekov - MD, Epilepsy Center, Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan, 80 Mangilik El Avenue, Astana, Kazakhstan,https://orcid.org/0009-0000-3291-362X

Mukhit Dosov - MD, Department of Anesthesiology and Intensive Care, Management Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan, 80 Mangilik El Avenue, Astana, Kazakhstan, https://orcid.org/0009-0000-3291-362X

Corresponding Author

AkmaralSuleimenova - MMS, Department of Science, Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan, 80 Mangilik El Avenue, Astana, Kazakhstan,https://orcid.org/0009-0001-2587-9248

Address: 80 Mangilik El Avenue, Astana 010000, Kazakhstan

E-mail: sulejmenovarajana5@gmail.com