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المجلة الصحية لشرق المتوسط

La Revue de Santé de la Méditerranée orientale

A well-coordinated, multisectoral approach is critical in addressing the broad range of risk factors, including those outside the health sector, associated with suicide in our communities

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المجلة الصحية لشرق المتوسط

هى المجلة الرسمية التى تصدر عن المكتب الإقليمى لشرق المتوسط بمنظمة الصحة العالمية. وهى منبر لتقديم السياسات والمبادرات الجديدة في الصحة العامة والخدمات الصحية والترويج لها، ولتبادل الآراء والمفاهيم والمعطيات الوبائية ونتائج الأبحاث وغير ذلك من المعلومات، وخاصة ما يتعلق منها بإقليم شرق المتوسط. وهى موجهة إلى كل أعضاء المهن الصحية، والكليات الطبية وسائر المعاهد التعليمية، وكذا المنظمات غير الحكومية المعنية، والمراكز المتعاونة مع منظمة الصحة العالمية والأفراد المهتمين بالصحة فى الإقليم وخارجه.

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Lives within reach: Suicide prevention in the Eastern Mediterranean Region

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Every year, more than 720 000 people die by suicide globally—the vast majority in low- and middle-income countries (*1*). In the WHO Eastern Mediterranean Region (EMR), over 27 000 lives were lost to suicide in 2021 alone. Seventy-one percent were male and nearly half were under the age of 30 years (*2*). Suicide remains the third leading cause of death among adolescents aged 15–19 years, and while rates have declined over 2 decades, the region is not yet on track to meet the United Nations Sustainable Development Goal of one-third reduction by 2030 (*1*). Behind every figure is a family shattered, a community diminished. These deaths are not inevitable—they are preventable.

The regional age-standardised suicide rate of 4.0 per 100 000 population is below the global average of 8.9, but aggregate figures conceal striking disparities (*1*). Country rates range from 0.7 per 100 000 in Jordan to 15.3 in Somalia, and in Pakistan, Islamic Republic of Iran and Libya, young adults bear a disproportionate burden. A regional situation analysis commissioned in 2023 identified mental health conditions, family history of suicide, interpersonal conflict, and domestic violence as key risk factors, and migrant workers, refugees and sexual and gender minorities as populations at higher risk (*4*).

Hanging, pesticide poisoning and self-immolation are the leading methods identified across the region (*4,5*), with poisoning—by pesticide and medication—particularly well-documented in Pakistan over several decades (*3,11*). Hospital-based surveillance consistently shows that deliberate self-harm clusters among adolescents and young adults, mirroring global trends (*3*).

The true burden of suicide is almost certainly greater than available figures suggest, given the widespread stigma attached to mental health conditions. Stigma tends to delay help seeking, compounded by criminalisation of suicidal behaviour and poor quality of data, resulting in deaths by suicide going unrecorded (*6*).

A public health response takes shape

The launch of LIVE LIFE initiative by WHO in 2021 provided countries with a practical, evidence-based framework on means restriction, responsible media reporting, life-skills development for young people, and strengthened mental health support, underpinned by multisectoral collaboration and robust surveillance (*7*).

Countries have responded with increasing resolve. Nine countries now have national suicide prevention strategies (*9*). Pakistan's 2022 decriminalisation of attempted suicide stands as a landmark—a fundamental shift from punishment to public health, removing barriers to care, reducing stigma, and laying the foundation for more accurate reporting (*6*). Pesticide bans have been established in 4 countries, with 6 training regulators, and life-saving potential of these interventions is well demonstrated in Bangladesh, China, Japan, Sri Lanka, and beyond (*7,8*).

Surveillance has advanced, with Pakistan strengthening self-harm monitoring and Islamic Republic of Iran developing a minimum data set to integrate suicidal behaviour data across systems (*9,10*). A media monitoring toolkit launched in 2023 helps governments to track adherence to WHO reporting guidelines, with training delivered in at least 7 countries (*12*). In schools, programmes such as Helping Adolescents Thrive and the Good Behaviour Game are building the socio-emotional skills that protect young people over a lifetime (*13*). At the community level, the WHO Mental Health Gap Action Programme (mhGAP) has been rolled out in at least 13 countries, equipping non-specialist health workers to assess and follow-up on people at risk. This is complemented by gatekeeper training in 7 countries and an online self-help module for those experiencing suicidal ideation or bereavement (*9,13*).

The road ahead

These gains are real—but they are fragile. The escalating conflict across the region threatens mental health infrastructure and compounds the very conditions—poverty, displacement and domestic violence—that drive suicidal behaviour. Sustaining the momentum requires clarity about what comes next.

Three priorities must guide our action. First, suicide data must improve. Without reliable surveillance, it is impossible to evaluate impact or respond to emerging trends; innovations underway in Pakistan and Islamic Republic of Iran offer models worth scaling-up across the region (*9,10*). Second, decriminalisation must remain a policy priority—legal frameworks that punish suicidal

behaviour obstruct care, reinforce stigma and undermine the data systems on which effective response depends (6). Third, suicide prevention must be recognised as a whole-of-government challenge. The determinants of suicidal behaviour—poverty, inequality, violence, social exclusion—extend far beyond the health sector and demand coordinated national strategies that bring policy-level action and evidence-based interventions under coherent leadership (4).

The EMR has demonstrated that progress is achievable. The task now is to accelerate that progress—ensuring that no country faces this challenge alone, that hard-won gains are not eroded by conflict or complacency, and that the goal of preventing 1 in 3 suicide deaths by 2030 moves from aspiration to reality.

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Potential and pitfalls of artificial intelligence application in medical diagnostics

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Artificial Intelligence (AI) has emerged as one of the most transformative innovations in healthcare, particularly in the field of medical diagnostics (*1*). By applying machine learning algorithms, deep learning models and access to large datasets, AI systems can detect patterns, interpret complex imaging and predict disease outcomes with remarkable accuracy (*2,3*). These advances have raised expectations for reducing diagnostic errors, improving efficiency and expanding access to care. In radiology, for example, AI has improved breast cancer screening sensitivity (*4*), while in pathology, deep learning tools have demonstrated accuracy comparable to human experts in histologic classification (*5*).

Despite these advances, AI adoption in clinical practice faces important challenges. Diagnosis is a complex process that requires not only data interpretation but also clinical expertise, contextual judgment and ethical responsibility. Real-world studies have shown that AI systems trained on homogeneous datasets may underperform in diverse populations, resulting in disparities in diagnostic accuracy (*6,7*). This issue is particularly relevant for the Eastern Mediterranean Region, where health systems are heterogeneous and data infrastructure remains underdeveloped.

During the COVID-19 pandemic, some countries in the region piloted AI-based triage systems to optimise resource allocation (*8*). However, limitations such as the lack of high-quality regional data, insufficient workforce trained in AI and weak regulatory frameworks continue to hinder effective integration (*9*). Therefore, although AI offers significant promise, its safe and effective use requires careful evaluation, local validation and investment in infrastructure and capacity building. This paper explores the potential and pitfalls of AI in medical diagnostics, with emphasis on the Eastern Mediterranean Region.

Complexity of diagnosis and the role of human clinicians

Diagnosis is not solely a matter of data analysis; it involves an intricate interplay of clinical expertise, patient history, physical examination and contextual understanding—factors that AI cannot fully replicate (*5*). The clinician's ability to interpret subtle clinical signs, comprehend patient narratives, appreciate psychosocial factors, and apply ethical reasoning remains central to quality care (*6*). Human empathy, communication and ethical responsibility are integral to the diagnostic process, shaping patient trust and adherence (*7*).

AI algorithms are typically trained on large datasets, which may lack diversity or regional specificity, limiting their generalisability (*8*). Biases inherent in training data can result in disparities in diagnostic accuracy across populations, raising concerns about equity and fairness (*9*). For the heterogeneous populations in the Eastern Mediterranean Region, with their varied genetic backgrounds, environmental exposures and disease patterns, AI tools developed elsewhere may underperform or yield misleading results if not properly adapted and validated locally (*10*).

For instance, a published case report described how overreliance on an AI dermatology tool resulted in the misclassification of a malignant lesion as benign, underscoring the importance of clinical correlation and physician expertise (*11*).

Risk of overreliance and deskilling

A critical pitfall is the potential for clinicians to over-rely on AI outputs, diminishing their own analytical skills and clinical reasoning over time. This "automation bias" can lead to acceptance of AI-generated diagnoses with inadequate scrutiny, risking the propagation of errors or overlooking atypical presentations (*12*). Maintaining clinical vigilance and fostering continuous education in critical thinking are essential to counterbalance this risk (*13*).

A systematic review reported that automation bias led clinicians to accept erroneous AI recommendations in nearly one-third of simulated diagnostic scenarios (*14*). More recent evaluations in radiology also confirmed that uncritical reliance on AI outputs increased the risk of overlooking atypical presentations (*15*).

Transparency and explainability

Many AI systems function as "black boxes," providing recommendations without transparent reasoning (*16*). This opacity challenges the ability of clinicians to understand, trust and justify AI-derived conclusions, complicating shared decision-making with patients. Recent developments in explainable AI, including methods such as the local interpretable model-agnostic explanations (LIME) and sHapley additive exPlanations (SHAP) have been proposed to provide clinicians with interpretable insights and improve accountability (*17*).

Ethics, legal and regulatory considerations

Responsibility for diagnostic decisions, patient safety and clinical outcomes remains with health care professionals. Ethical dilemmas emerge when AI errors cause harm, raising questions about liability and informed consent (*17*). Regulatory frameworks must evolve to address the unique challenges posed by AI, ensuring rigorous validation, quality control and patient data protection, especially in low-resource settings (*18*). International frameworks such as the European General Data Protection Regulation (GDPR), the United States Health Insurance Portability and Accountability Act (HIPAA), and the United States Food and Drug Administration (FDA) guidelines on AI/ML-based medical devices provide concrete examples of regulatory approaches that could inform regional policy development.

Infrastructure and capacity building

Successful AI implementation requires robust digital infrastructure, data governance and interoperability standards, which are often lacking in parts of the Eastern Mediterranean Region (*19*). The region faces major challenges due to the limited availability of large, valid and regionally representative datasets, which are essential for the safe deployment of AI systems. The shortage of a trained workforce familiar with AI and data science further constrains adoption. Recent reports by the WHO Regional Office for the Eastern Mediterranean emphasise the urgent need to build shared regional data repositories and capacity-building programmes tailored to the regional context. For example, Egypt has launched pilot projects in electronic health records, while Jordan and Lebanon continue to face difficulties in securing the necessary infrastructure and human resources (*20*). Investment in clinician training is paramount to empower health workers with the skills to interpret AI outputs critically and integrate them effectively into clinical workflows (*21*).

The path forward

To harness the full potential of AI, it is imperative to adopt a balanced, multidisciplinary approach. AI should complement, not replace, human clinical expertise, serving as an advanced decision support system. Collaborative efforts involving clinicians, data scientists, ethicists, and policymakers are essential to develop culturally sensitive, regionally validated AI tools tailored to local health care challenges (*20*).

In conclusion, although AI represents a revolutionary advancement with potential to improve diagnostic accuracy and health care delivery, it must be integrated thoughtfully and ethically, preserving the irreplaceable role of the human clinician. By embracing AI as an augmentative partner rather than a substitute, health systems in the Eastern Mediterranean Region can enhance patient outcomes while upholding the core values of medicine (21). To achieve this, policymakers should prioritise the development of regional data infrastructure and regulatory frameworks, health care leaders must invest in training programmes to prepare clinicians for AI integration, and researchers should generate empirical evidence and case studies tailored to the Eastern Mediterranean context. Only through such coordinated actions can AI be safely and equitably harnessed for the benefit of patients across the region (*21*).

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Funding, service and resource gaps at primary health care centres in Iraq

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Abstract

Background: Limited resources have hampered progress towards Universal Health Coverage at the primary health care level in Iraq.

Aim: To analyse the cost of primary health care services in Iraq and identify the resource gaps.

Methods: Using the CORE Plus tool, we collected and analysed data on finance and other resources, and services provided by 15 primary health care centres across 11 governorates in Iraq. We calculated the normative utilisation and cost estimates and compared them with the actual figures.

Results: Primary health care services were underutilised: only 52% (33–67%) of the 81 listed services were utilised across the 15 centres, and there was an average of only 1.2 visits per capita per year, compared with the estimated need of 4.5 visits. The expenditure incurred for the actual number of services was 2.5 times higher than the normative cost, due to over-staffing, despite shortages of medicines and supplies. The cost of meeting the need for 4.5 visits would be 21% more than the actual expenditure, but staffing costs would have to be reduced by 39% and medicines and supplies financing increased by 640%.

Conclusion: Funding for services at the primary health centres in Iraq was insufficient although the centres were overstaffed. To improve access and quality of services and progress towards Universal Health Coverage, staffing should be aligned with service needs and adequate resources provided.

Keywords: primary health care, health care, health resource, health finance, funding gap, staffing, UHC, Iraq

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Background

During the 1970s, the healthcare system in Iraq was considered one of the strongest in the Middle East (*1*). However, sustained reductions in public investment following periods of political instability and successive conflicts led to a substantial decline in service availability and quality (*1*). By 2003, the health system was operating under severe constraints, including malfunctioning equipment, inadequate drug supplies and weakened infrastructure. Although efforts were made during the 2003–2011 occupation to rebuild the system, weaknesses in governance and management limited progress (*1*).

In 2009, the Ministry of Health (MoH) introduced a Basic Health Services Package (BHSP) to improve service delivery from community to district hospital levels, and the package was updated in 2020 (*2*). A national health policy for 2014–2023 reaffirmed the government's commitment to progressing towards Universal Health Coverage (UHC), understood as access to needed good-quality health services without financial hardship. The policy included a strategic emphasis on strengthening primary health care (PHC) to improve access to basic services (*3–6*). As public sector service quality declined and the availability of medicines and equipment decreased, an increasing proportion of PHC services in Iraq was sought through largely unregulated private clinics, which were perceived as providing better quality care (*7*).

Implementation of the BHSP has been challenging, partly because it has been underfunded (*4*). The BHSP had not been costed previously, which limited the ability to allocate sufficient funding. To address this gap, in 2022, the MoH, with support from UNICEF, conducted a costing study of selected PHC centres and strengthened national capacity for PHC costing (*8*).

This paper reports the costing study, which aimed to estimate the normative cost of delivering the BHSP at an acceptable standard of quality, compare these estimates with actual expenditure, and identify the funding gap in efforts to achieve appropriate service coverage.

Methods

The costing methodology and tool used for this study were originally developed by Management Sciences for Health in 1995 for costing PHC packages. The tool, known as CORE Plus, has been widely used for PHC costing studies (*9–10*). CORE Plus was also included in an international review of PHC costing tools conducted in 2008 (*11*).

Data on services, resources and finances were entered into the tool to generate a model for each facility. The tool produced a set of reports analysing the data by service area, input category and programme, enabling comparisons of cost structures and resource requirements. A separate set of spreadsheets was linked to the facility models to compare the results across health centres and to generate the tables presented in this paper.

The methodology involved estimating the number of services needed and calculating the normative cost of delivering them. These results were then compared with the actual number of services provided and the expenditures incurred to determine the gaps (*12–13*). Only recurrent costs were included to allow comparison with government recurrent budgets and because capital costs are difficult to capture and project accurately.

Data were collected from 16 primary health care centres (PHCCs) and 2 sub-PHCCs, the main government PHC facility types. Data for 2019 were used because it was the most recent full year before COVID-19 had a major impact on service provision. This study complemented an immunisation costing study of 73 PHCCs conducted in 2019, and used a subset of those facilities (*14*).

For the immunisation study, facilities were stratified by region and selected through multistage probabilistic sampling. The 16 PHCCs selected for the present study were drawn from 12 of the 13 health directorates included in the earlier study, plus one additional directorate. Selection within each directorate was based on proximity to the main city or town for reasons of access and security. One PHCC lacked complete data and was excluded. The 2 sub-PHCCs were included in the costing analysis; however, their results are not reported separately because their operational characteristics differ from those of PHCCs. The remaining 15 facilities were distributed across 13 directorates in 11 governorates; 9 were in the Central and South Region, 2 in the Kurdistan Region of Iraq and 2 in the retaken areas. Of these, 9 facilities were in urban areas and 6 in rural settings.

Data on facility operations, service volumes, resources and finances were obtained from facility managers using a structured questionnaire. Normative staffing levels and costs for service delivery were based on standard treatment protocols developed using national and regional data and reviewed by a panel of medical experts. Standard salary and allowance rates were not available; therefore, actual rates from staffing lists were used.

Normative numbers of administrative and support staff (including diagnostic technicians and pharmacists) were not available; therefore, the normative costs for these categories of staff were assumed to be 27% of the total, based on the average actual proportion across the sampled facilities. Normative figures for non-staff operating costs were treated in the same way. The normative quantities of medicines and supplies were derived from the standard treatment guidelines, and the prices were based on government figures. The total facility operating costs were allocated across the services according to the total amount of technical staff time required to provide them.

The numbers of needed services were estimated using the facility catchment populations and the expected disease incidence and prevalence rates for curative services, and government targets for preventive services. It was assumed that the PHCCs should cover all needs for preventive services (such as vaccinations, which are only provided in the public sector in Iraq). For curative services, the estimates were adjusted to reflect the proportion of services delivered in the private sector.

Ethics approval

Ethics approval, confidentiality and data safeguarding were not required for this study because no confidential data were collected and no patients were interviewed.

Results

Facility information

Two of the urban facilities were open 24 hours a day. The other urban facilities were open for an average of 310 (290–365) days per year and 6.7 (6–8) hours per day, while the rural facilities were open for an average of 319 (263–358) days per year and 6 (5–7) hours per day. The average urban catchment population was 37 414, with 34 031 (13 901–70 000) for the urban facilities and 40 773 (15 000–85 000) for the rural facilities (*14*).

Service utilisation

The package for the PHCCs was defined as 81 services grouped into 8 programmes (Table 1). The number of services utilised at the PHCCs in 2019 ranged from 14 826 to 98 177, with an average of 45 114 (Table 1). This corresponded to 1.2 (0.6–2.3) services per capita, including 0.6 (0.2–1.4) for curative services and 0.6 (0.1–1.1) for preventive services.

Only 52% (33–67%) of the 81 listed services were utilised across the 15 PHCCs. Thirteen services were not reported by any PHCC, and some others were underreported. These included family planning counselling, contraceptive provision other than oral contraceptives, treatment of measles, sexually transmitted diseases, and screening for high cholesterol, breast and cervical cancer. It was not possible to determine whether these services were unavailable, available but not utilised, or underreported.

Vaccination services represented 35% of all utilisation, followed by communicable diseases (25%), child health (17%) and noncommunicable diseases (NCDs) (17%). There was significant variation across PHCCs: vaccinations ranged from 8% to 55%, communicable diseases from 14% to 42%, and NCDs from 3% to 33%.

The overall need for services across the public and private sectors was estimated at 5.6 per capita per year. Assuming that 63% of curative services and 100% of preventive services would be sought at PHCCs, the adjusted need was 4.5 services per capita per year (Table 1). This was significantly higher than the observed 1.2

Table 1 Average actual and needed utilisation figures for the main PHCCs, 2019

	Actual	Needed	With ranges Actual	With ranges Needed
Catchment population	37 414	37 414	37 414 (13 901–85 000)	37 414 (13 901–85 000)
Preventive services market share	100%	100%	100%	100%
Curative services market share	63%	63%	63% (25–100%)	63% (25–100%)
Proportion of service types provided	52%	100%	52% (33–67%)	100%
Number of services utilised	45 114	168 718	45 114 (14 826–98 177)	168 718 (52 849–395 345)
Number of preventive services	24 324	104 351	24 324 (4 226 –60 950)	104 351 (39 019–238 589)
Number of curative services	20 784	64 366	20 784 (7 334 –51 367)	64 366 (10 288–156 756)
Number of services per capita – total population	1.2	4.5	1.2 (0.6–2.3)	4.5 (3.5–5.6)
Number of preventive services per capita – total population	0.6	2.8	0.6 (0.1–1.1)	2.8 (2.5–2.8)
Number of curative services per capita – total population	0.6	1.7	0.6 (0.2–1.4)	1.7 (0.7–2.8)
Child health	17%	10%	17% (5–31%)	10% (9–12%)
Vaccination	35%	17%	35% (8–55%)	17% (14–23%)
Women's health	5%	3%	5% (2–9%)	3% (2–3%)
Family planning	0%	8%	0% (0–1%)	8% (6–10%)
Communicable diseases	25%	8%	25% (14–42%)	8% (4–10%)
Noncommunicable diseases	17%	44%	17% (3–33%)	44% (33–51%)
Emergency medicine	0%	0%	0%	0%
Public health	2%	11%	2% (0–20%)	11% (8–15%)

Small differences are due to rounding. Figures for the sub-PHCC and FHC are not included.

services per capita in 2019, indicating a large gap between expected and reported utilisation and suggesting that individuals may have sought care outside PHCCs or not sought formal care. Some counselling and screening services, such as family planning counselling, had 100% utilisation targets set by the MoH. If these targets were reduced from 100% to 20%, the overall utilisation rate would decrease to 3.6 services per capita per year.

Actual and normative costs for the PHCCs

The actual total expenditure in 2019 for the 15 sampled PHCCs ranged from US$ 281 026 to US$ 3 157 080, with an average of US$ 1 039 904 (US$ 23.05 per service and US$ 27.29 per capita for the catchment population) (Table 2). On average, technical staff costs accounted for 59% of total costs, support and administrative staff costs for 27%, medicines and supplies for 9%, and facility operating costs for 5%.

The average normative cost of providing the actual number of services was US$ 408 036, corresponding to US$ 9.04 per service and US$ 10.91 per capita (Table 2). This represented 39% of the actual expenditure, indicating that, on average, the PHCCs spent 2.5 times the amount needed. Across the PHCCs, actual expenditure ranged from 159% to 451% of the normative cost. This level of overspending was driven primarily by technical staff salary costs, which were, on average, 569% of the amount needed, and support and administrative salaries, which were 256% of the amount needed. In contrast, spending on medicines and supplies was only 67% of the amount needed. A total of 11 PHCCs underspent on medicines and supplies (26–85%), while 4 overspent (125–146%). Managers in 11 PHCCs reported medicine stockouts. Based on the normative costs for the actual number of services, the highest cost programme would have been NCDs (27%), followed by communicable diseases (26%), and child health (20%).

The higher technical staff expenditure observed in some facilities was primarily due to staffing levels that exceeded service requirements. Remuneration rates also varied widely; for example, average physician remuneration ranged from US$ 7376–32 617 (median US$ 13 352). A comparison of staffing lists with normative requirements showed that 7 PHCCs had more doctors than required, 12 had more dentists, 13 had more nurses, and 3 had more midwives. Three facilities had particularly large surpluses of technical staff. Requirements for ancillary, support and administrative staff could not be assessed because staffing norms were unavailable. However, 4 PHCCs appeared to have more laboratory technicians and one appeared to have more pharmacists. Support and administrative staffing levels also appeared to be high in some PHCCs. Despite these surpluses, 12 PHCCs reported shortages in other categories, such as dental assistants, indicating an imbalance between staffing composition and service delivery needs.

Table 2 Actual expenditures and normative costs for the sampled PHCCs, 2019

Cost data – average for main PHCCs	Actual services and actual expenditures	Actual services and normative costs	Needed services and normative costs
Total cost	US$ 1 039 903 (US$ 281 026–3 157 080)	US$ 408 036 (US$ 132 662–1 049 016)	US$ 1 262 411 (US$ 332 618–3 492 509)
Cost per service	US$ 23.05 (US$ 10.08–40.40)	US$ 9.04 (US$ 4.95–13.52)	US$ 7.48 (US$ 5.10–9.68)
Cost per capita – total population	US$ 27.29 (US$ 8.55–48.96)	US$ 10.91 (US$ 3.95–28.36)	US$ 33.74 (US$ 19.39–49.13)
Input costs			
Technical staff costs	59% (44–71%)	26% (16–35%)	34% (18–48%)
Support and administrative staff costs	27% (14–43%)	27% (16–37%)	9% (4–16%)
Medicines and medical supplies	9% (3–17%)	33% (21–52%)	52% (41–70%)
Facility operating costs	5% (1–18%)	14% (2–49%)	4% (1–17%)
Programme costs			
Child health	NA	20% (6–31%)	9% (6–11%)
Vaccination	NA	13% (2–30%)	6% (5–10%)
Women's health	NA	13% (5–35%)	5% (4–7%)
Family planning	NA	0% (0–1%)	6% (4–8%)
Communicable diseases	NA	26% (12–44%)	11% (9–14%)
Noncommunicable diseases	NA	27% (7–41%)	48% (36–54%)
Emergency medicine	NA	0%	0%
Public health	NA	1% (0–13%)	16% (12–23%)

Note: the figures in the needed services and normative costs column are for the needed services shown in Table 1.

Based on the projected need for 168 718 services for the average PHCC as shown in Table 1, the average recurrent cost would be US$ 1 262 411 (US$ 332 618–3 492 509), with an average of US$ 7.48 per service and US$ 33.74 per capita for the catchment population. Medicines and supplies would comprise 52% of this cost, technical staff 34%, administrative and support staff 9%, and operating costs 4%. Non-communicable diseases would represent 48% of the total cost, followed by public health (screening schoolchildren) (16%) and communicable diseases (11%).

Although the number of services would be approximately 4 times the actual number provided in 2019, the total required cost of US$ 1 262 411 is only 21% higher than the amount that was spent. However, to achieve the increased number of services, staffing costs would have to be reduced by 39% and medicines and supplies costs increased by 640%. If, as mentioned above, the targets for the five counselling and screening services were reduced from 100% to 20%, the average total projected cost would decrease by 17%.

Discussion

Although the number of sampled facilities was small, the findings are likely representative of conditions in many facilities across the country. Low utilisation has been repeatedly documented in previous studies, which have attributed this pattern to poor-quality services, long travel distances to health centres, and limited availability and affordability of medicines (*15–19*). Challenges in resource allocation have also been identified in other studies (*4,16,20,21*).

The large numbers of excess staff observed in this study can be partly explained by the national law enacted in 2000, which remained in force until 2024 and required the Ministry of Health to hire all graduates of health-related disciplines. The variation in excess staffing across facilities could not be explained, but may relate to the ethnic or religious composition of the workforce and the perceived advantages of particular locations. Although some publications have described shortages of health personnel, especially outside

major cities, these assessments may have been based on data from the 2014 National Health Policy document (*3*). Shortages at population level can coexist with excess staff at individual facilities if there are too few facilities or if facilities are unevenly distributed, preventing appropriate deployment. It is also possible that some staff allocated to PHCCs spent part of their time working in the private sector or in the afternoon fee-for-service clinics, a form of public dual practice that has long been reported in Iraq (*19,22,24*). Some staffing lists may have included individuals who were not actually present in the facilities, either as ghost workers or as staff formally assigned to multiple public facilities. Such issues are not uncommon in settings where corruption affects the public healthcare system (*25*).

The only other PHC costing study carried out in Iraq in recent years that could be compared with our findings was conducted by the MoH, but it was not publicly available. A national health accounts study published in 2018 also lacked cost data at the PHC level and therefore could not be used for comparison. Similar costing studies have been undertaken in other countries, but their results are not directly comparable because of differences in cost structures, data limitations, and the levels of resource inefficiency in Iraq (*27,28*).

The implications of the problems identified in this study are significant. Poorer patients who rely on PHCCs may not have sought care, delayed seeking care, or self-treated. Alternatively, they would have spent time and/or incurred travel costs to go to public hospitals, which may also have poor-quality services and medicines shortages, or to private providers, which could result in financial hardship (*22*).

Study limitations

The results of this study are subject to several limitations. Record-keeping at the health centres was incomplete and of poor quality, with almost no electronic data. Expenditure data for management and support functions and supplies were probably not complete at some facilities, although this would not have materially affected the results. For the normative cost estimates, the main areas of uncertainty relate to the challenges of calculating catchment populations and market share, as well as incidence and prevalence rates. The analysis did not include capital costs related to equipment or buildings, and did not assess constraints to scaling up, such as providing necessary equipment and expanding building space. The number of facilities was relatively small due to funding limitations and, while the selection of directorates was representative, the selection of facilities within the directorates was not random due to access and security constraints. The results reported in the paper were from the same type of facility, and while the facilities were located in both urban and rural areas, the designated package of services was the same and variations in catchment populations between them were not significant. Data checks were limited to querying outliers and adjusting for obvious errors. Tests for relationships were not conducted, and regression analysis was not considered worthwhile because of the quality of the data.

Given the small sample and these limitations, the results of the study should be regarded as illustrative, especially in relation to scaling up needs and related costs. However, the study provides insights into some of the challenges of managing and financing PHC in Iraq and supports the development of recommendations for improvement.

Conclusions

The analysis showed that there was insufficient funding to meet service needs at the health centres. It also showed that appropriate staffing would allow the reallocation of funding to medicines and supplies, which were underfunded. It is likely that these issues are widespread across the country and may persist despite the 2024 policy change on hiring. Furhter comprehensive research is needed to determine whether these issues persist and to provide a basis for the reallocation of resources.

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Five-year analysis of antibiotic consumption at university teaching hospitals in Tunisia

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Abstract

Background: A national antimicrobial consumption reporting system has been established in Tunisia, however, regional, hospital and departmental data on consumption remain limited.

Aim: To assess annual antibiotic consumption trends in Tunisia's university teaching hospitals from 2018 to 2022.

Methods: We analysed data on antibiotic consumption for 2018 to 2022 by patients aged ≥18 years admitted into 5 university teaching hospitals in Tunisia, based on the WHO defined daily doses per 1000 inhabitants per day and the access, watch and reserve classification. We assessed the differences between year, region, specialty and antibiotic classifications using the Friedman test. $P \leq 0.05$ was considered statistically significant.

Results: There was no significant difference in antibiotic consumption between the 5 hospitals over the 5-year period ($P = 0.455$). However, there were consistent significant differences between hospitals in the different regions and between antibiotic categories. There were significant differences in antibiotic consumption between the different hospital departments. The highest consumption was observed in the intensive care units (increasing from 154.2 defined daily doses per 1000 inhabitants per day in 2018 to 174.9 in 2022), which also had the highest increase in the consumption of reserve antibiotics (12.6% in 2018 to 16.7% in 2022).

Conclusion: The relatively stable antibiotic consumption observed in our study does not imply appropriate use. There is a need for robust antibiotic use surveillance systems in Tunisian hospitals, especially in intensive care units, alongside targeted interventions to effectively address antimicrobial resistance.

Keywords: antibiotic consumption, AWaRe classification, antimicrobial resistance, teaching hospital, Tunisia

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Introduction

Antimicrobial resistance (AMR) is one of the top 10 global public health threats identified by WHO, with projections suggesting it could cause up to 10 million deaths annually by 2050, potentially surpassing cancer as the leading cause of mortality worldwide (*1*). The clinical and economic burden is particularly severe in low- and middle-income countries, where multidrug-resistant bacteria are responsible for significantly higher mortality and substantial health care costs (*2,3*). Inappropriate and excessive use of antibiotics remains a major driver of AMR, with a strong correlation between antimicrobial consumption (AMC) and resistance rates (*4–6*). The COVID-19 pandemic has further exacerbated the crisis, as broad-spectrum antibiotics were widely prescribed despite limited evidence of bacterial co-infections (*7,8*).

In the WHO Eastern Mediterranean Region (EMR), the burden of AMR continues to increase alongside inappropriate use of antimicrobials (*9,10*). Tunisia, a lower middle-income country in North Africa comprising 24 governorates across 4 health regions, ranked second globally in antimicrobial consumption in 2015 (*11*). In response to the ranking, the country adopted a national action plan on AMR (2019–2023), developed in line with the WHO Global Action Plan. Key strategies include optimising AMC, strengthening surveillance systems, and implementing a national antimicrobial stewardship (AMS) programme that incorporates routine monitoring of AMC, use of the WHO AWaRe classification, and restrictions on prescribing 'reserve' antibiotics (*12,13*). This initiative includes a national AMC surveillance system and the adoption of the WHO's AWaRe classification, which groups antibiotics into 'access' (lower resistance potential), 'watch' (higher resistance potential) and 'reserve' (last-resort options for multidrug-resistant infections) categories (*14*). The AWaRe framework is designed to improve access to essential antibiotics while preserving their long-term effectiveness, with a global

target of at least 60% use of antibiotic consumption of the access group (*15*).

Accurate measurement of AMC is central to AMS efforts, as it helps identify misuse patterns, guides interventions, and assesses outcomes. WHO recommends the defined daily dose (DDD) methodology, expressed as DDD per 1000 inhabitants/day for community settings and per 100 patient-days for hospitals (*16,17*). In Tunisia, national-level AMC decreased from 38 DDD/1000 inhabitants/day in 2015 to 27.98 in 2022 (*18*). However, regional and hospital-level surveillance, particularly in university teaching hospitals, remained limited (*19,20*). Understanding AMC patterns in these hospitals is essential for evaluating stewardship initiatives and promoting rational antibiotic use (*21*).

This study, therefore, aimed to assess and compare annual AMC trends expressed as DDD/100 patient-days, by region, AWaRe classification, pharmacological subgroups and hospital department specialities, among adult inpatients in Tunisia's public university hospitals from 2018 to 2022 in Tunisia.

Methods

Study setting

The Tunisian healthcare system, divided into 4 regions – Greater Tunis, northern, central, and southern regions – is predominantly public sector (76% of the total hospital beds) (*22*). All university teaching hospitals belong to the public sector and provide free treatment.

Tunisia has 24 tertiary-level university hospitals with a total bed capacity of 10 570 (*22*). This study was conducted in 5 major teaching hospitals, with more than 3500 beds, selected to ensure geographic representation across all the 4 health regions. One hospital each from Greater Tunis, northern, and central regions was chosen based on bed capacity and availability of medical, surgical, and intensive care departments. For the southern region, 2 hospitals (one medical and one surgical) were included, to ensure balanced speciality coverage. These hospitals are key regional referral centres providing specialised and tertiary care.

The pharmacy departments of these 5 hospitals implemented AMS activities, including prescription restrictions for reserve antibiotics and pharmaceutical validation of antibiotic prescriptions.

Study design

This was a cross-sectional study that assessed annual AMC in 5 university teaching hospitals in Tunisia. The study included all adult (aged ≥18 years) inpatients admitted to the 5 selected hospitals for whom drug procurement data were available from 2018 to 2022. To estimate AMC, only systemic antibiotics (ATC group J01) were included. Anti-tuberculosis drugs and locally administered antibiotics were excluded in accordance with WHO surveillance methodology (*23*). Outpatients, dialysis patients, and those treated in day hospitals were excluded. Patients admitted to psychiatric, physical medicine, re-education, and functional rehabilitation departments were also excluded because of the high number of patient-days in these units, which could lead to an underestimation of antibiotic consumption when expressed as DDD per 100 patient-days. Paediatric patients were also excluded, because their DDD calculation methods differ from those for adults.

Data included antibiotic details (code, denomination, international nonproprietary name, pharmacological class, dosage, form, and AWaRe category), the number of units procured, and patient-days per department. AMC rates were expressed as DDD per 100 patient-days and categorised using AWaRe classification, pharmacological subgroup, region, and department speciality from 2018 to 2022. Specific clinical indications were not available in aggregated pharmacy data, therefore, analysis by department was used as a proxy for likely treatment categories. Departments were grouped as surgical (e.g. general, cancer, cardiovascular surgery), medical (e.g. oncology, cardiology, nephrology), intensive care (medical and surgical ICUs), and gynaecological–obstetric.

AMC data were obtained through hospital-based pharmacy surveillance systems in each participating hospital. All pharmacy departments use a centralised drug management software developed by the Ministry of Health's Computer Centre. This tool records medication dispensing – including antibiotics – based on electronic or handwritten prescriptions for hospitalised patients. Each dispensed antibiotic is logged by drug code, quantity, and hospital department, enabling continuous tracking of inpatient antibiotic use. Patient-days data, used to calculate standardised consumption rates, were sourced from annual administrative reports provided by each hospital's statistics unit.

Each pharmacy department generated Microsoft Excel files from the hospital's pharmacy software, aggregating antibiotic consumption by department and year. These reports, automatically produced during routine dispensing, included units dispensed with audit-trail details (time, patient, dosage). Files were named using a standardised "year_department" convention and organised by hospital. Bed-days data from hospital administration were entered and double-checked.

All datasets were then compiled into a central advanced Excel template using PowerQuery®, which added year and department variables, flagged aberrant values, and ensured a uniform data structure. This template also automated DDD and DDD per 100 patient-days calculation, minimising manual handling to enhance accuracy. To further ensure validity, 20% of the entries were manually cross-checked against original records using WHO-recommended manual DDD calculations.

Antibiotic consumption was estimated using the WHO methodology for AMC surveillance. The DDD is defined as the average maintenance dose per day of an antimicrobial substance used for its main indication in adults (*23*). To standardise antibiotic use across varying

patient loads and hospital sizes, we calculated DDD per 100 patient-days, which reflects the amount of antibiotics consumed per 100 days of inpatient care (17).

Data analysis

DDD per 100 patient-days was calculated for each antibiotic and stratified by year, region, speciality, AWaRe category and pharmacological class. Percentage consumption was calculated as each antibiotic's share of total DDD/100 patient-days (%). Differences between years, regions, AWaRe classification, pharmacological classes and specialities were assessed using the Friedman test. Statistical significance was set at $P \leq 0.05$ and 95% confidence intervals.

Ethics considerations

Approval for this study was obtained from the Heads of Pharmacy Department, the Institutional Review Board of Sahloul University Hospital, Sousse, Tunisia (HS 12–2024) and the Union Ethics Advisory Group at the International Union against Tuberculosis and Lung Disease, Paris, France (EAG No. 02/24). As this study used aggregate institutional data from routine records, a waiver of informed consent was approved.

Results

Overall annual antibiotic consumption

In the 5 participating hospitals, antibiotic consumption (DDD/100 patient-days) was 51.4 in 2018, 49.4 in 2019, 52.3 in 2020, 51.1 in 2021 and 49.9 in 2022, with no statistically significant differences over time ($P = 0.455$). The proportion of access antibiotics was 51.7% in 2018, compared with 45.9% for watch and 2.4% for reserve. By 2022, this had changed to 47.5% for access, 48.7% for watch, and 3.8% for reserve (Figure 1).

Table 1 summarises trends in consumption by pharmacological class and AWaRe category. In 2018, the 5 most used antibiotic classes were beta-lactam/beta-lactamase inhibitors (11.2 DDD/100 patient-days), third-generation cephalosporins (7.1 DDD/100 patient-days), penicillins (6.9 DDD/100 patient-days), fluoroquinolones (5.2 DDD/100 patient-days), and carbapenems (5.0 DDD/100 patient-days). By 2022, beta-lactam/beta-lactamase inhibitors remained the most consumed class (10.9 DDD/100 patient-days), followed by third-generation cephalosporins (7.0 DDD/100 patient-days), carbapenems (6.0 DDD/100 patient-days), fluoroquinolones (4.6 DDD/100 patient-days), and aminoglycosides (4.6 DDD/100 patient-days). Carbapenems increased from fifth place in 2018 to third in 2022, while penicillins decreased from third to seventh.

Three of the 5 most consumed antibiotics in 2022 – third-generation cephalosporins, carbapenems, and fluoroquinolones – were in the watch group. Access antibiotic use decreased from 26.5 DDD/100 patient-days in 2018 to 24.1 DDD/100 patient-days in 2022. Watch antibiotic use remained stable over the study period, with a slight increase in 2020. In contrast, the use of reserve antibiotics increased from 1.2 to 1.9 DDD/100 patient-days between 2018 and 2022, mainly due to higher colistin consumption.

Antibiotic consumption by region

The regional trends showed consistent differences between hospitals over the 5 years (Figure 2a). In 2022, the lowest consumption was recorded in Region 1 (30.0 DDD/100 patient-days) and Region 2 (50.1 DDD/100 patient-days), while higher levels were observed in Region 3 (53.0 DDD/100 patient-days) and Region 4 (62.4 DDD/100 patient-days).

Regional AWaRe patterns also varied: in 2022, regions 1 and 2 reported higher proportions of access antibiotics (> 50%), while regions 3 and 4 recorded lower proportions (< 50%) (Figure 2b).

Antibiotic consumption by department speciality

Table 2 shows variations in consumption by department. In medical departments, AMC decreased from 41.5 DDD/100 PD in 2018 to 34.2 DDD/100 patient-days in 2022. In contrast, surgical departments showed higher and increasing consumption, from 52.6 to 56.4 DDD/100 patient-days over the same period. In gynaecology-obstetrics, antibiotic use decreased from 50.3 to 39.4 DDD/100 patient-days.

The highest consumption was observed in ICUs, increasing from 154.2 to 174.9 DDD/100 patient-days. Surgical ICUs reached a peak of 194.8 DDD/100 patient-days in 2020. AMC differed significantly between ICUs and gynaecology/obstetrics, medical and surgical departments ($P < 0.001$).

AWaRe patterns by department showed ICUs had the highest and increasing proportion of reserve antibiotics (12.6% in 2018 to 16.7% in 2022), with access antibiotics consistently below 33%. Gynaecology-obstetrics had the highest access proportions (90% in 2018 and 87% in 2022) (Figure 3). In surgical specialities, access antibiotics accounted for <54% of use throughout the period, while in medical specialities, the proportion decreased from 43.9% in 2018 to 39.5% in 2022.

Discussion

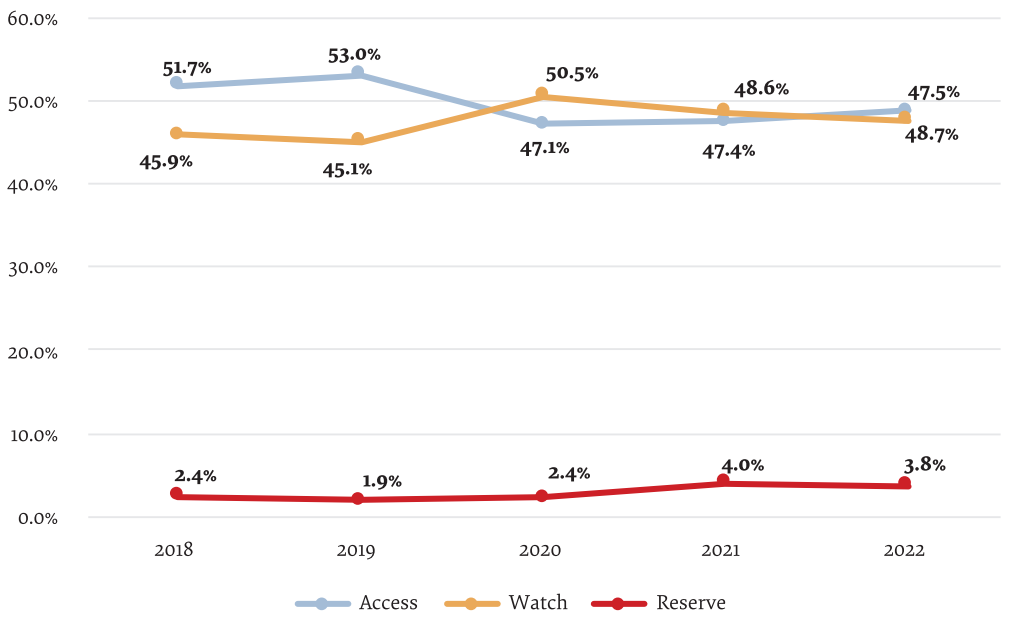
Overall AMC in the 5 participating university teaching hospitals remained relatively stable between 2018 and 2022, ranging from 51.4 to 49.9 DDD/100 patient-days, although regional variations were noted. ICUs consistently reported the highest levels of antibiotic use, with AMC increasing from 154.2 to 174.9 DDD/100 patient-days over the same period. The most commonly used antibiotic classes were beta-lactam/beta-lactamase inhibitors, third-generation cephalosporins, and carbapenems, with the latter's increasing use raising particular concern. ICUs had the lowest proportion of access antibiotic use and the highest proportion of reserve antibiotic use, which increased from 12.6% in 2018 to 16.7% in 2022, primarily due to increased colistin use. This pattern suggests intensive and potentially excessive antibiotic use, likely driven by a

Table 1 Antibiotic consumption in defined daily dose per 100 patient-days by pharmacological class and AWaRe category, Tunisia, 2018–2022

AWaRe category/pharmacological class		Defined daily dose/100 patient-days				
		2018	2019	2020	2021	2022
Access	Penicillin	6.9	5.9	3.6	3.5	2.7
	First generation cephalosporins	1.0	1.1	1.2	0.6	1.2
	Beta-lactam/beta-lactamase-inhibitor	11.2	11.0	10.5	11.6	10.9
	Aminoglycosides	2.5	3.3	4.7	4.4	4.6
	Tetracyclines	0.5	0.6	0.3	0.0	0.0
	Lincosamides	0.1	0.2	0.2	0.2	0.4
	Imidazoles	3.9	3.5	3.8	3.4	3.8
	trimethoprim-combinations	0.4	0.4	0.3	0.4	0.5
	Total access	**26.5**	**26.0**	**24.6**	**24.1**	**24.1**
Watch	Third generation cephalosporins	7.1	6.9	8.2	7.7	7.0
	Carbapenems	5.0	5.0	5.5	5.5	6.0
	Glycopeptides	2.3	1.8	2.5	2.7	3.2
	Fluoroquinolones	5.2	4.8	5.1	4.9	4.6
	Macrolides	0.9	1.0	2.6	1.7	0.7
	Rifamycins	1.9	1.8	1.6	1.2	0.9
	Beta-lactam/beta-lactamase-inhibitor	0.7	0.5	1.0	1.0	1.3
	Steroid antibacterials	0.5	0.3	0.1	0.1	0.0
	Total watch	**23.6**	**22.1**	**26.6**	**24.8**	**23.7**
Reserve	Glycylcyclines	0.38	0.42	0.31	0.57	0.50
	Polymyxins	0.67	0.42	0.85	1.39	1.26
	Oxazolidinones	0.05	0.03	0.03	0.03	0.05
	Phosphonics	0.12	0.06	0.03	0.04	0.08
	Total reserve	**1.2**	**0.9**	**1.2**	**2.0**	**1.9**

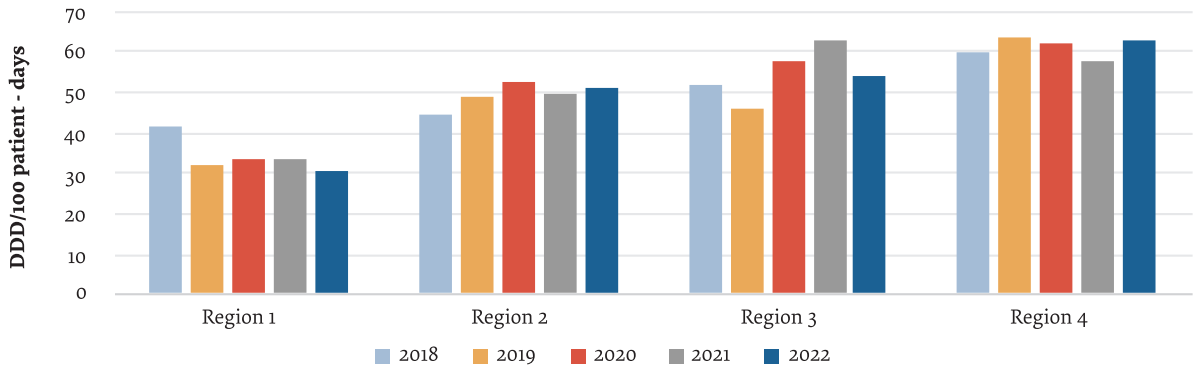
AWaRe = access, watch, reserve categories of antimicrobials

Figure 1 Annual antibiotic consumption by AWaRe category at university teaching hospitals, Tunisia, 2018–2022



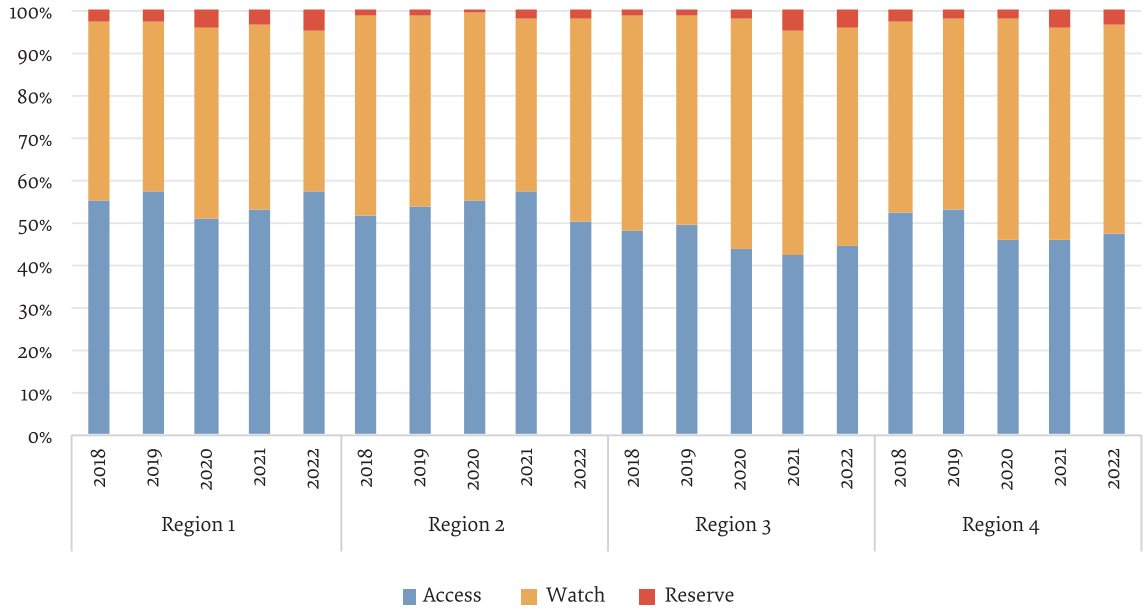
*AWaRe = access, watch and reserve categories of antimicrobials

Figure 2a Antibiotic consumption at university teaching hospitals (defined daily dose per 100 patient-days) by region, Tunisia, 2018–2022



AWaRe = access, watch, reserve categories of antimicrobials

Figure 2b Antibiotic consumption at university teaching hospitals (defined daily dose per 100 patient-days) by region and AWaRe category, Tunisia, 2018–2022



AWaRe = access, watch, reserve categories of antimicrobials

high prevalence of health care-associated infections and multidrug-resistant bacteria. These findings highlight the urgent need for targeted AMS interventions, particularly in high-use settings such as ICUs.

This study provides the first multicentre, department-based analysis in Tunisia comparing AMC patterns across regions. A previous single-centre study in Greater Tunis (2010–2022) reported lower access, watch and reserve antibiotic use than our findings (18.51 DDD/100 patient-days for access, 17.37 DDD/100 patient-days for watch, and 1.41 DDD/100 patient-days for reserve in 2022) (*19*).

For context, a Qatari hospital reported an AMC of 228.9 DDD/100 bed-days, while a multicentre survey in 14 Turkish hospitals found 67.45 DDD/100 patient-days. A 6-year study in a secondary-level facility in Ghana reported 86.18 DDD/100 patient-days (*24–26*). Similarly, a systematic review of antimicrobial use in West Africa highlighted substantial AMC variation (*27*). While these levels exceed those reported in our study (≈ 50 DDD/100 patient-days), contextual differences – particularly hospital setting, clinical activity, patient mix, and AMS implementation – must be considered. Our study involved teaching hospitals with established AMS and senior prescribers, who likely promote more rational

Table 2 Trends of antibiotic consumption (defined daily dose per 100 patient-days) at university teaching hospitals in Tunisia (2018-2022), stratified by department specialities

Department specialities		AWaRe category	Annual antibiotic consumption (defined daily dose per 100 patient-days)					*P*
			2018	2019	2020	2021	2022	
Medical		Access	18.2	16.2	14.2	11.5	13.5	0.006
		Watch	22.8	21.0	27.6	23.0	20.2	
		Reserve	0.5	0.5	0.5	0.4	0.5	
		Total	**41.5**	**37.7**	**42.3**	**34.9**	**34.2**	
Surgical		Access	27.0	26.0	28.5	30.7	28.6	0.006
		Watch	25.0	23.6	25.9	26.1	26.6	
		Reserve	0.6	0.5	0.8	0.9	1.2	
		Total	**52.6**	**50.1**	**55.2**	**57.7**	**56.4**	
Gyneco-obstetrics		Access	45.4	49.0	31.1	34.1	34.3	0.006
		Watch	4.9	5.6	4.8	4.6	5.0	
		Reserve	0.0	0.0	0.0	0.0	0.1	
		Total	**50.3**	**54.6**	**35.9**	**38.7**	**39.4**	
Subtotal: Non-ICU departments		Access	25.6	24.8	22.8	22.8	23.1	0.014
		Watch	21.3	20.0	23.6	21.7	21.0	
		Reserve	0.5	0.5	0.6	0.6	0.8	
		Total	**47.2**	**45.3**	**47.0**	**45.1**	**44.9**	
ICU	**Medical ICU**	Access	44.1	51.7	42.5	32.5	46.8	0.006
		Watch	89.4	88.0	96.8	83.8	83.5	
		Reserve	20.6	11.7	13.2	26.9	25.5	
		Total	**154.1**	**151.4**	**152.5**	**143.2**	**155.8**	
	Surgical ICU	Access	56.8	67.3	85.2	73.0	60.1	0.014
		Watch	79.1	70.8	80.8	88.9	99.0	
		Reserve	18.4	13.5	18.6	32.9	32.6	
		Total	**154.3**	**151.6**	**184.6**	**194.8**	**191.7**	
Subtotal ICU departments		Access	51.2	60.7	65.9	51.9	54.1	0.006
		Watch	83.6	78.1	88.0	86.3	91.6	
		Reserve	19.4	12.7	16.2	29.8	29.2	
		Total	**154.2**	**151.5**	**170.1**	**168.0**	**174.9**	

ICU = intensive care unit; AWaRe = access, watch, reserve categories of antimicrobials

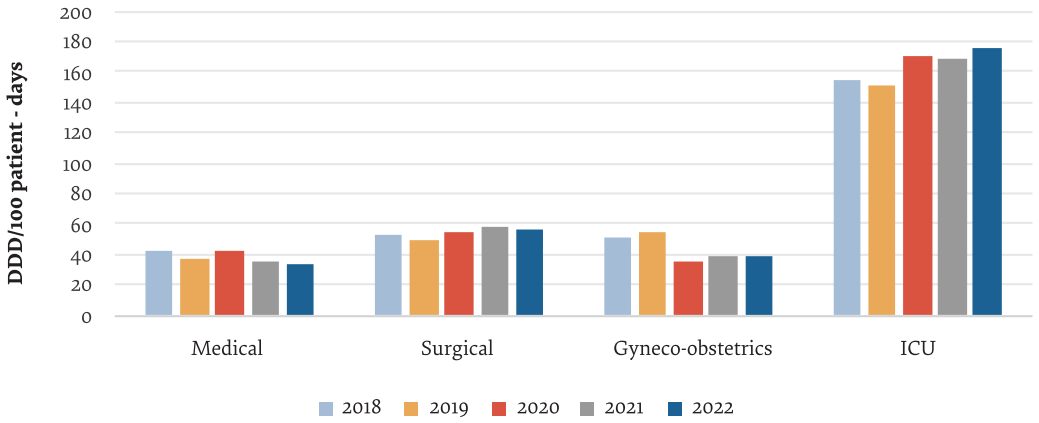
antibiotic use. Although prescriber behaviour was not assessed, it remains a critical determinant of AMC. These findings underscore the need to interpret AMC data within comparable institutional contexts for meaningful benchmarking.

AMC distribution by AWaRe classification varied significantly across departments, with ICUs showing the highest total reserve use. This pattern aligns with a Tunisian prevalence survey and a Turkish study, both of which found ICU admission to be associated with higher antibiotic consumption (*20,25*). Access antibiotics accounted for less than 50% of total use across all participating hospitals, decreasing below 31% in ICUs by 2022. Nationally, Tunisia met the WHO target of ≥ 60% access antibiotic consumption, although a 2024 UN high-level meeting proposed a 70% target (*18,28*). However, in tertiary hospitals with ICUs and surgical services managing complex, resistant infections, achieving such thresholds may be unrealistic, underscoring the need for context-specific benchmarks.

The high consumption of watch antibiotics, particularly of third-generation cephalosporins, fluoroquinolones, and carbapenems, is concerning and aligns with findings from other studies in Tunisia and the broader region (*19,20,24,25*). Of particular concern is the increasing use of carbapenems and colistin, alongside decreasing penicillin use. This pattern is likely linked to increasing extended-spectrum beta-lactamase resistance, carbapenemase-producing enterobacterales, and a high burden of health care-associated infections in Tunisian tertiary hospitals (*29,30,20*). The COVID-19 pandemic may have further fuelled empirical antibiotic use without confirmed bacterial infections.

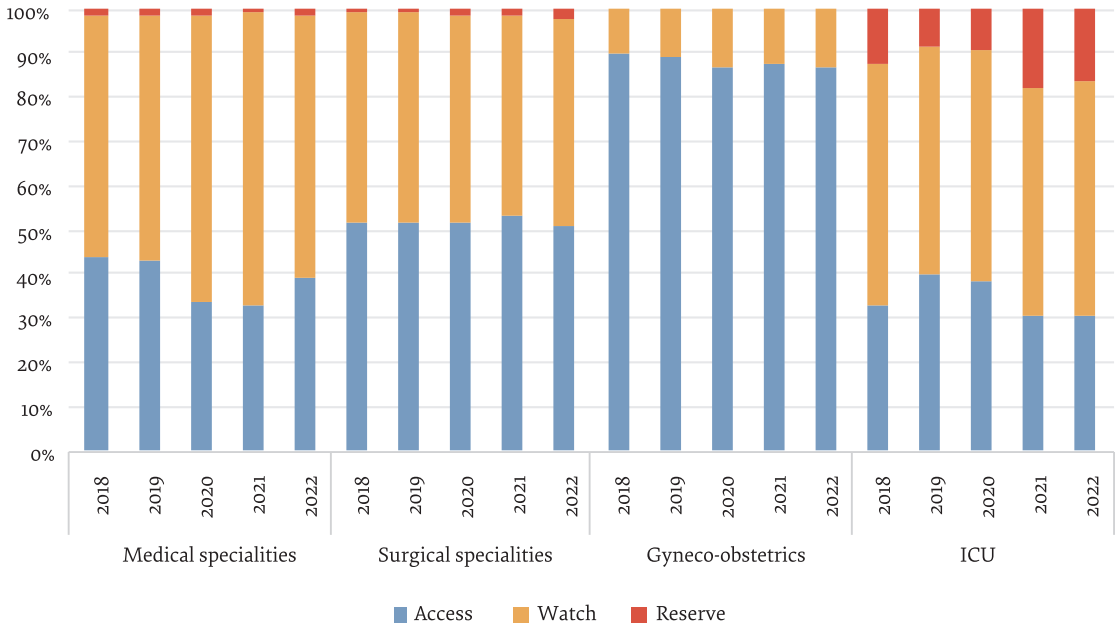
The strengths of this study include its multicentre, department-based design, inclusion of university hospitals from all Tunisian regions, and combined use of quantitative (DDD/100 patient-days) and qualitative (AWaRe) metric, as

Figure 3a Antibiotic consumption at university teaching hospitals (defined daily dose per 100 patient-days) by department speciality, Tunisia, 2018–2022



AWaRe = access, watch, reserve categories of antimicrobials

Figure 3b Proportion of antibiotic consumption at university teaching hospitals (%) by AWaRe category and department speciality, Tunisia, 2018–2022



AWaRe = access, watch, reserve categories of antimicrobials; ICU = intensive care unit

recommended by WHO (17). The study followed STROBE guidelines (17,31).

The study limitations include the exclusion of primary/secondary facilities as well as private hospitals, limiting generalisability; potential underestimation of AMC due to exclusion of certain long-stay departments; and lack of patient-level clinical data, which limited the analysis of prescribing indications. To address the last 2 limitations, we excluded departments with long hospital stays and applied a consistent calculation method to minimise bias.

Despite these limitations, this study highlights consistently high antibiotic use in ICUs, low access proportions, and increasing carbapenem consumption, which represent critical targets for AMS in Tunisia.

We recommend establishing a standardised national surveillance system that adopts both DDD/100 patient-days and the AWaRe indicators. Tracking antibiotic consumption at hospital and departmental levels will enable targeted antimicrobial stewardship interventions. Priority actions include optimising antibiotic use in ICUs, where consumption is highest, and strength-

ening infection prevention and control to reduce health care-associated infections. The increasing use of carbapenems calls for stricter indication validation and improved therapy duration management through routine prescription monitoring and clinician awareness. Future surveillance should integrate electronic prescription with diagnostic coding to capture patient-level clinical indications. COVID-19 related antibiotic data should be incorporated, as post-pandemic prescription may affect resistance trends. These measures are essential for data-driven AMS and informed national AMR policy.

Conclusion

Our study provides a national baseline, showing relatively stable antibiotic consumption in university teaching hospitals in Tunisia from 2018 to 2022. However, stability does not equate appropriate antibiotic use. Persistent challenges, particularly the high use of watch and reserve antibiotics in ICUs, highlight the need for robust surveillance at all hospitals. These findings underscore the urgency of targeted antimicrobial stewardship interventions and sustained investment in national surveillance systems to effectively address AMR.

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Multidrug resistance and mortality in patients with hospital-acquired urinary tract infections in Islamic Republic of Iran

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Abstract

Background: Hospital-acquired urinary tract infections are a frequent complication in intensive care units. They are increasingly being associated with multidrug-resistance, especially in low-resource settings.

Aim: To assess the uropathogenic and antimicrobial resistance patterns and identify patient-related factors associated with multidrug resistance and mortality among patients with hospital-acquired urinary tract infections in Tehran, Islamic Republic of Iran.

Methods: We analysed secondary data on all patients aged ≥ 18 years who had hospital-acquired urinary tract infections and were admitted to intensive care units of 45 public and private hospitals in Tehran, Islamic Republic of Iran, between 2022 and 2024. We examined the associations between the demographic and clinical variables using prevalence ratios and the outcomes of interest using relative risks. $P \leq 0.05$ was considered statistically significant.

Results: Of the 2467 patients, 60% were catheterised. A bacterial pathogen was isolated from 77% and *Candida* spp. from 23%. The most common pathogens were *Escherichia coli* (26%), *Klebsiella* spp. (22%) and *Candida* spp. (23%). Seventy-two percent of 1590 patients assessed exhibited multidrug resistance. Males, catheterised patients and patients with extended catheter use (> 8 days) had higher prevalence of multidrug resistance. Overall mortality rate was 42% and mortality was highest among patients with prolonged catheter use (57%), those admitted in public hospitals (51%) and those infected with *Candida spp* (60%).

Conclusion: The alarmingly high prevalence of multidrug resistance and high mortality rate among patients with hospital-acquired urinary tract infections indicate the need to enhance infection prevention and control practices in Iranian hospitals, and to significantly improve antibiotic susceptibility testing and antimicrobial resistance surveillance.

Keywords: hospital-acquired urinary tract infection, catheter-associated urinary tract infection, multidrug resistance, antimicrobial resistance, intensive care units, mortality, Islamic Republic of Iran.

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Background

Health care-associated infections (HCAIs) are infections acquired by patients while receiving care in a health care facility, and they represent the most frequent adverse events occurring during health service delivery (1).

A 2023 systematic review estimated the global prevalence of HCAIs at 14%, with the highest burden reported in the African Region (27%) and the lowest in the Region of the Americas (9%) (2). Rates were substantially higher in low-income (32%) and middle-income countries (16%) than in high-income countries (6%), consistent with the findings of the 2022 WHO global report on infection prevention and control (3).

While HCAIs occur in all health care settings, they are more common among patients admitted to intensive care units (ICUs) due to underlying disease, immunosuppression, and the use of invasive devices (4). A 2023 review estimated that 68% of ICU patients, globally, developed HCAIs, more than double the 30% reported in the 2011 WHO report (1,25).

Data on the burden of HCAIs in Islamic Republic of Iran are limited. A 2018 national surveillance analysis reported an incidence of 4.2 per 1000 patient-days, with substantial variations among universities, hospitals and departments (6). ICU-associated infection rates were higher, at 16.8 per 1000 patient-days, with pneumonia and urinary tract infections (UTIs) identified as the most prevalent types (7). Among device-associated in-

fections, ventilator-associated pneumonia (VAP) was most common, followed by catheter-associated urinary tract infections (CAUTIs). Overall mortality attributed to HCAIs was 15.7%, although this is likely an underestimation due to reliance on passive surveillance (*7,8*).

UTIs are among the most frequently reported HCAIs, affecting between 20 and 50% of ICU patients (*9*). Horizontal transfer of resistance genes among uropathogens poses a significant challenge to treatment and infection control in these settings (*10*). The most common causes of UTI include *Escherichia coli* (*E.coli*), *Klebsiella* spp., *Citrobacter* spp, *Proteus mirabilis*, *Pseudomonas* spp., *Enterococcus* spp., *Staphylococcus saprophyticus* and *Candida* spp. (*11*).

Previous studies from Islamic Republic of Iran on hospital-acquired UTIs have typically been single-centre, with limited sample sizes, and have often focused on the specific resistance patterns of a single pathogen (*12–16*). Studies examining risk factors for multidrug resistance (MDR) – defined as resistance to 3 or more classes of antibiotics and mortality are scarce (*17*). While national reports provide a broad overview, they remain insufficient for guiding decision-making at the hospital level. Given the wide variation in the burden and resistance patterns of hospital-acquired UTIs across hospitals, up-to-date local data are essential for instituting effective hospital-level policies on treatment and antibiotic selection.

Accordingly, we undertook this operational research among patients with hospital-acquired UTIs admitted to the ICUs of hospitals within the jurisdiction of Iran University of Medical Sciences between 2022 and 2024, to determine: (i) the types of pathogens isolated and their antibiotic resistance patterns; (ii) the proportion of cases with MDR and associated mortality; and (iii) demographic and clinical factors associated with MDR and mortality.

Methods

Study setting

Islamic Republic of Iran is located in the WHO Eastern Mediterranean Region, with a population of approximately 84 million and a per capita gross domestic product (GDP) of US$ 4400, classifying it as a lower-middle-income country (*18*). The country has 1066 hospitals, 75% of which are public. Licensing and accreditation are managed by medical universities in coordination with the Ministry of Health and Medical Education (MOHME).

This study was conducted in 45 hospitals within the jurisdiction of Iran University of Medical Sciences (IUMS), one of the leading academic institutions in Tehran, the capital city. These included 7 public academic hospitals, 5 public non-academic hospitals and 33 private hospitals. Most of them were tertiary-level hospitals, with a few offering secondary care services. The facilities were geographically distributed from the northwest to the southwest of Tehran. Some hospitals operated more than one ICU, categorized as surgical ICU, medical ICU, paediatric ICU and neonatal ICU.

Upon admission to ICU, patients underwent a comprehensive physical examination and baseline laboratory tests including haematology, biochemistry, urinalysis, urine culture and antimicrobial susceptibility testing, as appropriate. Urine samples are taken only from patients with symptoms suggestive of UTI, or when clinically warranted at the discretion of the attending physician.

As per national guidelines, which are closely aligned with the criteria of the United States Centers for Disease Control and Prevention/National Healthcare Safety Network (CDC/NHSN), catheter-associated urinary tract infection (CAUTI) is defined as a UTI in a patient with an indwelling urinary catheter in place for more than 48 hours prior to the onset of symptoms. The patient must exhibit at least one of the following: fever (temperature > 38°C), urgency, frequency, dysuria, suprapubic pain or costovertebral pain/tenderness. Positive urine culture was defined as ≥ 105 colony-forming units (CFU)/mL involving no more than 2 isolated species. Hospital-acquired urinary tract infection was defined as a UTI occurring ≥ 48 hours after hospital admission, presenting with the above symptoms (*19*). Asymptomatic bacteremic UTI was defined as the absence of urinary symptoms with concurrent positive urine and blood cultures for the same uropathogen.

All participating hospitals had microbiology laboratory capabilities to perform antimicrobial susceptibility testing. Culture and testing were conducted manually using the disk diffusion method, following national protocols aligned with the Clinical and Laboratory Standards Institute (CLSI) 2024 guidelines (*20*). Antibiotics were tested against identified organisms and results were reported as susceptible, intermediate or resistant.

Candida spp. were considered clinically significant only if they met national diagnostic criteria, including both clinical symptoms and a urine culture of ≥ 105 CFU/mL. Asymptomatic bacteriuria was included only when associated with positive blood cultures suggestive of urosepsis, consistent with national surveillance definitions.

Minimum inhibitory concentration (MIC) testing was performed for resistant organisms when available, while molecular resistance testing was limited to selected hospitals for research purposes.

Study design

This was a retrospective analysis of secondary data collected as part of the national surveillance-based cohort study.

Every hospital was staffed with an infection prevention and control (IPC) nurse responsible for the documentation and reporting of HCAIs, in line with the guidelines of the Iranian nosocomial infection surveillance (INIS) system. INIS was launched in 2007 and scaled up nationally, with ≈98% of hospitals participating as of 2023. Two standardised forms were used: Form 1(individual case form) capturing demographic, clinical and laboratory data, and Form 2 collecting denominator data (e.g.

patient-days, device-days) for incidence calculation. Data were submitted monthly into the INIS database by the IPC nurse. Then, they were compiled and analysed centrally by the Iranian Centre for Disease Control at MOHME.

We included all patients with hospital-acquired UTIs admitted to ICUs of public and private hospitals operating within the jurisdiction of IUMS between 2022 and 2024.

From the INIS database, we extracted the following data on each patient: age, sex, catheterisation status and duration (interval between catheter insertion and infection), ICU type, infection duration (interval between symptom onset/sample collection and discharge or death), isolated uropathogens, antimicrobial resistance patterns, and mortality.

Data analysis

Data were exported from the INIS database into Microsoft Excel and analysed using Stata version 16.0. Categorical variables were summarised as frequencies and percentages, and continuous variables as medians and interquartile ranges (IQR). Associations between demographic and clinical variables and the outcomes of interest (MDR and mortality) were examined using prevalence ratios and relative risks, respectively, with 95% confidence intervals (CIs), calculated via modified Poisson regression.

All available variables were retained in the multivariable model, after assessing and excluding collinearity. Variables included in the MDR analysis were age, sex, hospital sector (public or private), ICU type, symptom status, comorbidities, referral status, catheterisation, catheter duration, and pathogen. Variables included in the mortality analysis were age, sex, hospital sector, ICU type, symptom status, comorbidities, referral status, catheterisation and MDR status.

$P \leq 0.05$ was considered statistically significant.

Ethics approval

Ethics approval was obtained from the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease (11/24, dated 02-02-2024) and the Institutional Ethics Committee of Iran University of Medical Sciences (IR.IUMS.REC.1402.1046, dated 02-07-2024). Permission to access data was obtained from MOHME officials. This study complied with the Declaration of Helsinki and national data protection regulations, using secondary data from INIS, which included only medical records. The study was observational and had no impact on patient care. The dataset was fully anonymised, ensuring no personally identifiable information was included. Access was restricted to authorised researchers, to prevent unauthorized use or manipulation.

Results

Demographic and clinical characteristics

Table 1 shows the demographic and clinical characteristics of the study population. Of the 2467 patients included, 1318 (53%) were female. The median age was 71 years (IQR: 58–81). A total of 1154 patients (47%) were admitted to ICUs in private hospitals. Asymptomatic bacteriuria was identified in 322 patients (13%). Overall, nearly half of the patients had at least one comorbidity, and 277 (11%) were referred from other hospitals.

Catheter-associated urinary tract infections

A total of 1479 patients (60%) were catheterised, of whom approximately 75% were catheterised on the day of admission or earlier, in the case of referred patients. The median duration between catheterisation and infection was 8 days (IQR: 2–18). Overall, the median time from hospital admission to onset of infection was 6 days (IQR: 1–16), and from admission to outcome (death or discharge) was 18 days (IQR: 9–35).

Common uropathogens and resistance patterns

A bacterial pathogen was isolated in 1891 patients (77%), while *Candida* spp. was identified in the remaining 565 (23%). Among the bacteria, *E. coli* (26%) was the most common pathogen, followed by *Klebsiella* spp. (22%), *Pseudomonas* spp. (10%), *Enterococcus* spp. (7%) and *Acinetobacter* spp. (4%). Table 2 presents the number of bacterial isolates tested for susceptibility and resistance across different antibiotic classes. The proportion tested varied from 0% to 85%, depending on the organism and antibiotic class. Among those tested, high levels of resistance were observed across most antibiotic groups.

Multidrug resistance

Of the 1891 patients with bacterial UTI, 301 (12%) were not assessed for MDR, because they had not been tested for at least 3 classes of antibiotics. Among the remaining 1590 patients, 1148 (72%; 95% CI: 70–74%) were found to have MDR. Multivariable analysis (Table 3) showed that males had a higher prevalence of MDR than females. Patients who were catheterised – particularly those with catheterisation exceeding 8 days – had significantly higher MDR prevalence than non-catheterised patients. Among bacterial isolates, *Acinetobacter* spp. had the highest prevalence of MDR (97%), followed by *Pseudomonas aeruginosa* (90%), *Klebsiella* spp. (80%) and *Enterobacter* spp. (79%).

Mortality

Outcome data were missing for 19 patients. Among those whose outcomes were recorded, 1024 (42%, 95% CI: 40–44%) died, and the rest were discharged. Multivariable analysis (Table 4) indicated that mortality was significantly higher among patients who had been catheterised for more than 8 days prior to infection. Patients infected with *Candida* or other fungal pathogens had the highest risk of mortality compared with those infected with non-MDR bacteria. Mortality was also higher among patients admitted to public hospitals than among those in private hospitals.

Table 1 Demographic and clinical characteristics of patients with hospital-acquired urinary tract infections admitted to the intensive care units of hospitals within the jurisdiction of Iran University of Medical Sciences, 2022–2024

Characteristic	N	%
Age (years)		
< 15	77	3.1
15–59	583	23.6
≥ 60	1807	73.2
Sex		
Male	1147	46.5
Female	1318	53.4
Not recorded	2	0.1
Sector		
Private	1154	46.8
Public	1313	53.2
Type of ICU		
Medical ICU	1868	75.7
Surgical ICU	506	20.5
NICU and PICU	93	3.8
Symptom		
Asymptomatic	322	13.0
Symptomatic	2145	87.0
Comorbidities		
Present	1123	45.5
Absent	1344	54.5
Referral from external facility		
Yes	277	11.2
No	2190	88.8
Urinary catheterisation		
Yes	1479	59.9
No	988	40.1
Organism isolated		
Escherichia coli	634	25.7
Klebsiella spp.	552	22.4
Pseudomonas	258	10.5
Enterococcus spp.	177	7.2
Acinetobacter	104	4.2
Staphylococcus spp.	54	2.2
Enterobacter	34	1.4
Candida	565	22.9
Others*	89	3.6
Not Recorded	19	0.8
Total	**2467**	**100**

*Others included Citrobacter, Chlamydia sp., Burkholderia, Proteus, other viruses and fungi.
**ICU = intensive care unit; MICU = medical ICU; SICU = surgical ICU; NICU = neonatal ICU; PICU = paediatric ICU

Discussion

This study contributes to the existing evidence base in Islamic Republic of Iran regarding the predominant uropathogens responsible for hospital-acquired UTIs in ICUs, their antimicrobial resistance patterns, including MDR and associated mortality. Four key findings emerged. First, approximately 60% of patients with UTIs were catheterised. Second, the most commonly isolated uropathogens were *E. coli*, *Candida* spp., *Klebsiella* spp. and *Pseudomonas aeruginosa*. Third, around 70% of patients were infected with MDR organisms, with MDR significantly associated with sex, catheter use, duration of catheterisation and bacterial species. Fourth, mortality was 42%

Table 2 Testing and resistance levels among the common bacterial isolates of patients with hospital-acquired urinary tract infections admitted to the intensive care units of hospitals within the jurisdiction of Iran University of Medical Sciences, 2022–2024

Drug class	*E coli* (n = 634)		*Klebsiella* (n = 552)		*Pseudomonas* (n = 258)		*Enterococcus* (n = 177)		*Acinetobacter* (n = 104)	
	Number tested	Resistance %	Number tested	Resistance %	Number tested	Resistance %	Number tested	Resistance %	Number tested	Resistance %
Macrolides	13	92	11	91	0	–	23	96	0	–
Cephalosporins	538	77	451	85	215	90	22	86	74	95
Penicillin	75	81	61	97	35	94	118	79	15	93
Tetracycline	89	55	98	65	65	94	47	83	43	72
Glycopeptides	N/A	N/A	N/A	N/A	N/A	N/A	136	67	N/A	N/A
Fluoroquinolones	487	69	429	82	199	85	114	82	71	93
Carbapenem	446	22	390	67	212	84	27	59	69	94
Betalactams	265	57	224	83	154	89	10	40	53	85
Aminoglycosides	525	32	449	64	209	78	56	64	72	85
Oxazolidines	N/A	N/A	N/A	N/A	N/A	N/A	111	6	N/A	N/A
Chloramphenicol	52	12	64	64	46	93	7	29	14	100
Sulfonamide	303	71	256	79	93	0	24	75	40	75
Nitrofurantoin	456	14	378	68	94	98	111	10	38	97
Rifamycin	0	–	0	–	0	–	11	82	0	–

*N/A = not applicable

(more than 4 out of every 10 patients), highlighting the severity of these infections.

Catheter use and the duration of catheterisation remain the most important factors in the development of bacteriuria (*21*). In a study by Tasseau et al, each day of catheterisation increased the risk of developing UTI by 5%, depending on the most common species and its antibiogram, with almost all patients being colonised by day 30 (*22*). A previous study from Islamic Republic of Iran reported an MDR prevalence of 85.9% in catheter-associated UTIs in ICUs, consistent with our findings (*23*).

MDR prevalence was higher among males than females. This may be associated with structural abnormalities such as urolithiasis and comorbidities like benign prostatic hypertrophy, common in elderly males associated with poor drainage of urine, as well as the use of long-term indwelling catheters, which complicate infection eradication and prolonged antibiotic use, potentially leading to the development of resistance (*24*). MDR levels were higher in public hospitals than private hospitals. This pattern may reflect overcrowding in relatively under-resourced public hospitals with possibly suboptimal IPC practices. This requires further research. The common uropathogens identified in our study are consistent with other studies from Islamic Republic of Iran and elsewhere, with minor variations in the relative proportions (*22,24–27*).

Mortality in our study was 42% – substantially higher than reported in a previous study from Islamic Republic of Iran (*28*). Previous studies from different countries have reported various mortality rates: USA (2.3%), Peru (19%), Germany (27%), India (28%), Tunisia (33%), and Sweden (42%) (*29*). *Candida* was isolated in about 25% of patients in our study and these patients had a higher risk of mortality (60%) than those with UTIs caused by bacteria (32%). This may reflect the underlying immunocompromised state of the patients and the presence of comorbidities. We did not have information about the species of *Candida* or their resistance patterns to different classes of antifungals. With the emergence of resistant 'superbugs' such as *Candida auris*, information about species and resistance patterns is crucial to inform effective treatment options.

In our study, longer catheterisation duration was associated with higher mortality. Previous studies have reported conflicting findings on catheter-associated UTI and mortality, with one study reporting no association (*30*) and another reporting an independent association with mortality (*31*). This warrants further research.

Other reported risk factors for mortality include: age, length of stay in the ICU, central line days, mechanical ventilator use ratio, central line-associated bloodstream infection acquisition, ventilator-associated pneumonia acquisition, female sex, and hospitalisation in a public hospital (*30*). We found higher mortality in public hospitals than in private hospitals; the reasons for this difference are unclear and require further investigation.

Our study had several strengths. We included all hospitals, including those in the private sector, within the jurisdiction of the Iran University of Medical Sciences, making the findings representative of the area covered. The large sample size enabled robust analysis of factors associated with MDR. Use of routine surveillance data for this operational research means the findings reflect the realities in Islamic Republic of Iran. We reported the study in accordance with the STROBE guidelines (*32*).

Table 3 Factors associated with multidrug resistance among patients with hospital-acquired urinary tract infections admitted to the intensive care units of hospitals within the jurisdiction of Iran University of Medical Sciences, 2022–2024 (n = 1590)*

Characteristic	Total	MDR		Adjusted		*P*
		N	%	PR	(95% CI)	
Age (years)						
< 15	52	38	73	1.10	(0.88–1.38)	0.384
15–59	386	273	71	Ref		
≥ 60	1152	837	73	1.06	(0.99–1.14)	0.090
Sex						
Male	731	568	78	1.09	(1.03–1.16)	0.003
Female	857	579	67	Ref		
Not recorded[$]	2	1	50	–	–	
Sector						
Private	723	507	70	Ref		
Public	867	641	74	1.10	(1.02–1.18)	0.005
Type of ICU						
Medical ICU	1221	867	71	1.01	(0.83–1.24)	0.888
Surgical ICU	296	230	78	1.05	(0.86–1.30)	0.621
NICU and PICU	73	51	70	Ref		
Symptom						
Asymptomatic	195	144	74	1.08	(0.98–1.19)	0.106
Symptomatic	1395	1004	72	Ref		
Comorbidities						
Present	717	524	73	1.03	(0.97–1.09)	0.355
None	873	624	71	Ref		
Referral from external facility						
Yes	236	173	73	1.09	(0.99–1.20)	0.056
No	1354	975	72	Ref		
Urinary catheterisation						
Yes (≤ 8 days)	530	375	71	1.12	(1.04–1.22)	0.002
Yes (> 8 days)	342	298	87	1.28	(1.20–1.37)	< 0.001
No	718	475	66	Ref		
Organism isolated						
Acinetobacter	76	74	97	1.76	(1.32-2.33)	< 0.001
E. coli	554	317	57	1.08	(0.81-1.44)	0.595
Enterobacter	24	19	79	1.42	(1.02-1.99)	0.039
Enterococcus spp.	142	97	68	1.23	(0.91–1.66)	0.187
Klebsiella spp.	446	374	80	1.49	(1.12–1.99)	0.006
Others	65	47	72	1.32	(0.96–1.82)	0.085
Pseudomonas	218	196	90	1.63	(0.96–1.82)	0.001
Staphylococcus spp.	45	24	53	Ref		
Total	**1590**	**1148**	**72**			

**N = number of bacterial isolates for which sensitivity results for at least 3 antibiotic classes were available to make an inference on MDR status; #Row percentage; [$]Excluded from regression analysis; MDR = multidrug resistant hospital acquired urinary tract infection (any bacteria that shows resistance to ≥ 3 antibiotic groups); ICU = intensive care unit; PICU = paediatric intensive care unit; NICU = neonatal intensive care unit; CI = confidence interval; Ref = reference category*

The study had some limitations, including missing data on the results of antibiotic resistance, either due to no testing or no documentation. As a result, in about one-third of patients, we could not assess MDR status. Data on comorbidities and other clinical variables were not recorded because the national guidelines, limit detailed analysis of mortality. Given the retrospective nature of this study, there was no access to other potential variables, such as the presence of central line-associated bloodstream infections, ventilator-associated pneumonia, or history of immunosuppressive drug use, which may have been important in analysing factors associated with mortality.

Table 4 Factors associated with mortality among patients with hospital-acquired urinary tract infections admitted to intensive care units of hospitals within the jurisdiction of Iran University of Medical Sciences, 2022–2024 (n = 2448)

Characteristic	Total	Mortality		Adjusted		*P*
		N	%	PR	(95% CI)	
Age (years)						
< 15	77	12	16	Ref		
15–59	581	233	40	1.43	(0.67–3.08)	0.356
≥ 60	1790	779	43	1.71	(0.80–3.65)	0.164
Sex						
Male	1137	488	43	1.01	(0.93–1.11)	0.799
Female	1309	536	41	Ref		
Not recorded[§]	2	0	0			
Sector						
Private	1140	358	31	Ref		
Public	1308	666	51	1.55	(1.37–1.76)	< 0.001
Type of ICU						
Medical ICU	1852	780	42	1.98	(0.95–1.14)	0.067
Surgical ICU	503	231	46	1.79	(0.86–3.75)	0.120
NICU and PICU	93	13	14	Ref		
Symptom						
Asymptomatic	321	118	37	Ref		
Symptomatic	2127	906	43	0.79	(0.66–0.94)	0.007
Comorbidities						
Present	1113	479	43	1.08	(0.98–1.18)	0.115
None	1335	545	41	Ref		
Referral from external facility						
Yes	275	71	26	Ref		
No	2173	953	44	1.60	(1.28–1.99)	
Urinary catheterisation						
Yes (≤ 8 days)	786	294	37	1.00	(0.88–1.14)	0.945
Yes (> 8 days)	687	395	57	1.36	(1.20–1.54)	< 0.001
No	975	335	34	Ref		
MDR						
Bacteria (MDR)	1141	452	40	1.15	(0.99–1.35)	0.069
Bacteria (Non-MDR)	440	139	32	Ref		
Bacteria (MDR not assessed)	293	88	30	1.04	(0.83–1.30)	0.745
Candida and other non-bacteria	574	345	60	1.44	(1.22–1.69)	< 0.001
Total	**2448**	**1024**	**42**			

[§]*Excluded from regression analysis given low number of patients; ICU = intensive care unit; NICU = neonatal intensive care unit; PICU = paediatric intensive care unit; CI = confidence interval; N/A = not applicable; Ref = reference category*

Although these limitations should be considered, the findings have important implications. First, we recommend strengthening data recording. This may require sensitisation and training of IPC nurses, who are responsible for recording and reporting surveillance data at the hospital level. Second, high levels of MDR in hospital-acquired UTIs indicate continuous nosocomial transmission and the need to strengthen IPC practices in ICUs. Third, data on antibiotic resistance patterns reported in this study can be used to inform the choice of antibiotics in empirical therapy of UTIs, while awaiting drug susceptibility results. The national clinical guidelines should be tailored at the hospital level based on periodic analysis of local surveillance data. Antibiotic stewardship committees in the respective hospitals should take the lead in this direction. Fourth, every bacterial isolate should be tested against a panel of antibiotics as recommended national and international standards. This was not always the case. The proportion tested for susceptibility varied across drug classes, being suboptimal in some instances and inappropriate in others, for example, by using incorrect antibiotics to test the bacteria. This reflects challenges in access to quality-assured supplies, issues in procurement and supply chain management of laborato-

ry consumables, and non-adherence to laboratory protocols. These issues need to be addressed. We recommend instituting testing for *Candida* speciation and antifungal susceptibility.

Conclusion

In this study covering both public and private hospitals within the jurisdiction of Iran University of Medical Sciences, we found alarming levels of MDR and mortality among patients with hospital-acquired UTIs. MDR was significantly higher among males, catheterised patients, and those infected with bacteria such as *Acinetobacter, Klebsiella* and *Pseudomonas*. Mortality was associated with extended catheterisation, public hospitals, and infection with fungal pathogens. Several operational issues related to suboptimal levels of antibiotic susceptibility testing and data recording were identified. These need to be addressed urgently to enable the generation of high-quality surveillance data and periodic analysis, thereby informing tailored treatment for patients in the university hospitals.

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Epidemiologic analysis of rabies cases among humans in Iraq

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Abstract

Background: Rabies is a fatal acute viral encephalitis that remains a public health problem in Iraq. There is continuous reported transmission nationwide.

Aim: To describe the epidemiology of reported rabies cases from 1997 to 2024 among humans in Iraq.

Methods: We collected data on all reported probable cases of rabies among humans for 1997–2024, from the Iraq national rabies surveillance database. We analysed the data using SPSS version 27 and Microsoft Excel 2019, and calculated the incidence rates per 10 million population.

Results: A total of 437 rabies cases were reported during the period, with an annual mean of 15.6 ± 6.6 cases. Cases occurred throughout the year, with a relative peak between May and October. The highest number of cases was reported in 1999 (30 cases; 6.9%) and the lowest was in 2015 (6 cases; 1.4%). Most cases occurred among children aged <15 years (60.2%), and males accounted for 82.2% of cases. The highest incidence rates per 10 million population were reported in the central and southern governorates, particularly Babylon (11.18) and Diyala (10.99).

Conclusion: Iraq continues to report a high number of rabies cases among humans annually. To achieve the WHO target of eliminating rabies among humans by 2030, there is a need for more effective rabies control measures, including better stray dog population management, expanded animal vaccinations, improved public awareness, and continuous access to rabies vaccines and immunoglobulin.

Keywords: rabies, stray dog, vaccination, vaccine, immunoglobulin, Iraq

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Background

Rabies is a widespread acute viral encephalitis that causes nearly 59 000 human deaths each year worldwide, although the real burden is likely underreported. Once clinical symptoms appear, rabies is almost invariably fatal (*1*). The disease is transmitted from wild and domestic animals to humans, and children aged < 15 years account for approximately 40% of the cases (*2*). The incubation period is usually 2–3 months (range: one week to one year). Clinical manifestations include hyperactivity or, less frequently, paralysis, hallucinations, lack of coordination, hydrophobia, and aerophobia. Rabies deaths are preventable with prompt post-exposure prophylaxis, including wound washing, administration of rabies vaccine, and, when indicated, rabies immunoglobulin. Additional preventive measures include dog vaccination and bite prevention (*3*).

Rabies has been reported in neighbouring countries such as Saudi Arabia, Jordan and Oman (*4*). The disease has a long history in Iraq, with scattered reports documenting rabies in wildlife. However, the prevalence of rabies in wildlife and its role in the transmission to humans remain poorly understood. All Iraqi governorates are considered at risk, and most reported human cases occur among children aged < 15 years and among males (*5*).

In recent decades, thousands of dog bites have been reported annually in Iraq, and rabies cases have been widely reported throughout the country. Despite limited human and financial resources and prolonged periods of conflict since 2003, rabies control efforts have continued to some extent, mainly through intersectoral campaigns focusing on stray dog culling. Veterinary services have implemented additional rabies control measures, including vaccination of animals. However, the vaccination coverage rate remains unknown (*6*). Routine surveillance records are the only available national data source and rely on regular reporting from all governorates.

This study describes the long-term epidemiology of reported rabies cases among humans in Iraq from 1997 to 2024, including temporal trends, sociodemographic characteristics, and geographical and seasonal distribution.

Methods

Study design and data source

A cross-sectional study was conducted using data from the national routine rabies surveillance system for the period 1997–2024. The study was based on a compatible clinical presentation and a history of animal exposure. Laboratory confirmation after death is not

routinely performed because autopsy is not permitted for suspected infectious cases under national forensic regulations (7). Laboratory confirmation before death is also not routinely available. Cases with inconclusive diagnoses or those subsequently diagnosed as conditions other than rabies were excluded.

The national surveillance system includes immediate case notification and routine monthly reporting from zoonotic units in all governorates using a standardised case investigation form, with data compiled in Excel spreadsheets. Data are transmitted electronically to the central level and analysed centrally. Variables available for analysis include age, sex, governorate, and month of case occurrence. Data are routinely reviewed at the central level for completeness and consistency.

Case definitions

National rabies case definitions were applied (*8*). Suspected cases are cases that are compatible with the clinical case definition of acute encephalitis, presenting as either hyperactive (furious rabies) or paralytic rabies and progressing to coma and death. Clinical features may include aerophobia, hydrophobia, paresthesia or localised pain, localised weakness, dysphagia, nausea, or vomiting. Probable cases are suspected cases with reliable history of contact with a suspected, probable, or confirmed rabid animal. Confirmed cases are suspected or probable cases confirmed by laboratory testing.

Earlier versions of the surveillance system did not capture variables such as residence or occupation and were limited to basic sociodemographic characteristics, including age and sex; the system has since been updated.

Data analysis and presentation

Incidence rates per 10 million population were calculated using national population statistics (*9*).

Data were analysed using SPSS version 27 and Microsoft Excel 2019. Records were anonymised using serial identification numbers. Descriptive statistics were used to summarise the data, including frequencies and percentages for categorical variables and means and standard deviations for continuous variables. Results were presented using tables, graphs and maps.

Ethics considerations

Data were anonymised and used exclusively for research purposes. Ethics approval was obtained from the ethics and scientific committee of the Ministry of Health.

Results

The study included 437 rabies cases among humans reported between 1997 and 2024. The annual number of cases ranged from 6 to 30, with a mean of 15.6 ± 6.6 cases per year (Figure 1). The highest numbers of reported cases were observed in 1999 (30 cases; 6.9%), followed by 2005 (29 cases; 6.6%), 2009 (27 cases; 6.2%) and 2010 (23 cases; 5.3%). The lowest numbers were reported in 2015 (6 cases; 1.4%), followed by 2001 (7 cases; 1.6%), with 2012 and 2013 each reporting 8 cases (1.8%).

In terms of geographical distribution, Baghdad reported the highest number of cases (75; 17.2%), followed by Babylon (57; 13.0%), Ninewa (49; 11.2%), and Diyala (47; 10.8%). Duhok did not report any cases. Sulaimaniya and Kirkuk each reported 5 cases (1.1%) and Al-Najaf reported 7 cases (1.6%), as shown in Figure 2. The national incidence rate was 4.63 cases per 10 million population. At the governorate level, the highest incidence rates per 10 million population were reported in Babylon (11.18), followed by Diyala (10.99), Kerbela (8.38), Maysan (8.37), and Al-Muthana (7.11), while the lowest rates were observed in Duhok (0), Sulaimaniya (0.91), Kirkuk (1.34), and Al-Najaf (1.98), as shown in Figure 3.

Children aged < 15 years accounted for 263 cases (60.2%), while 174 cases (39.8%) occurred among individuals aged ≥ 15 years. Males accounted for 359

Figure 1 Annual distribution of reported rabies cases among humans in Iraq, 1997–2024

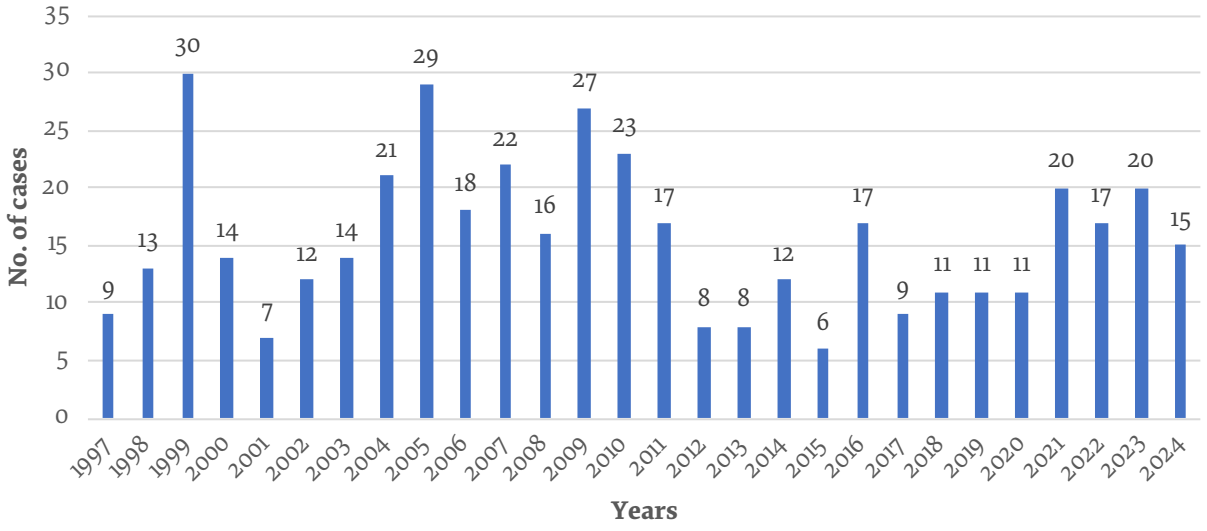
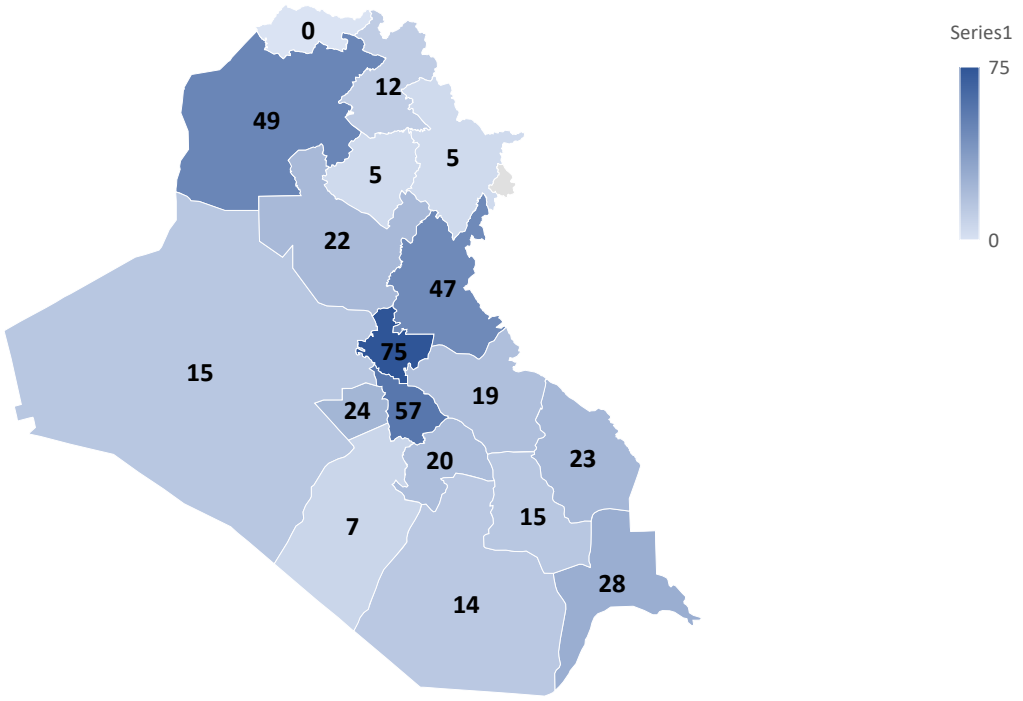


Figure 2 Distribution of reported rabies cases among humans by governorate, Iraq, 1997–2024



cases (82.2%), and females for 78 cases (17.8%), as shown in Table 1.

Cases were reported throughout the year, with a relative peak during the summer and autumn months (May to October), as shown in Figure 4.

Discussion

A total of 437 rabies cases among humans were reported in Iraq over a 28-year period (1997–2024). The annual number of cases ranged from 6 to 30, with a mean of 15.6±6.6 cases per year. According to WHO, rabies remains endemic across 150 countries and territories worldwide, with approximately 95% of human deaths occurring

Figure 3 Incidence rate of rabies cases per 10 million human population by governorate, Iraq, 1997–2024

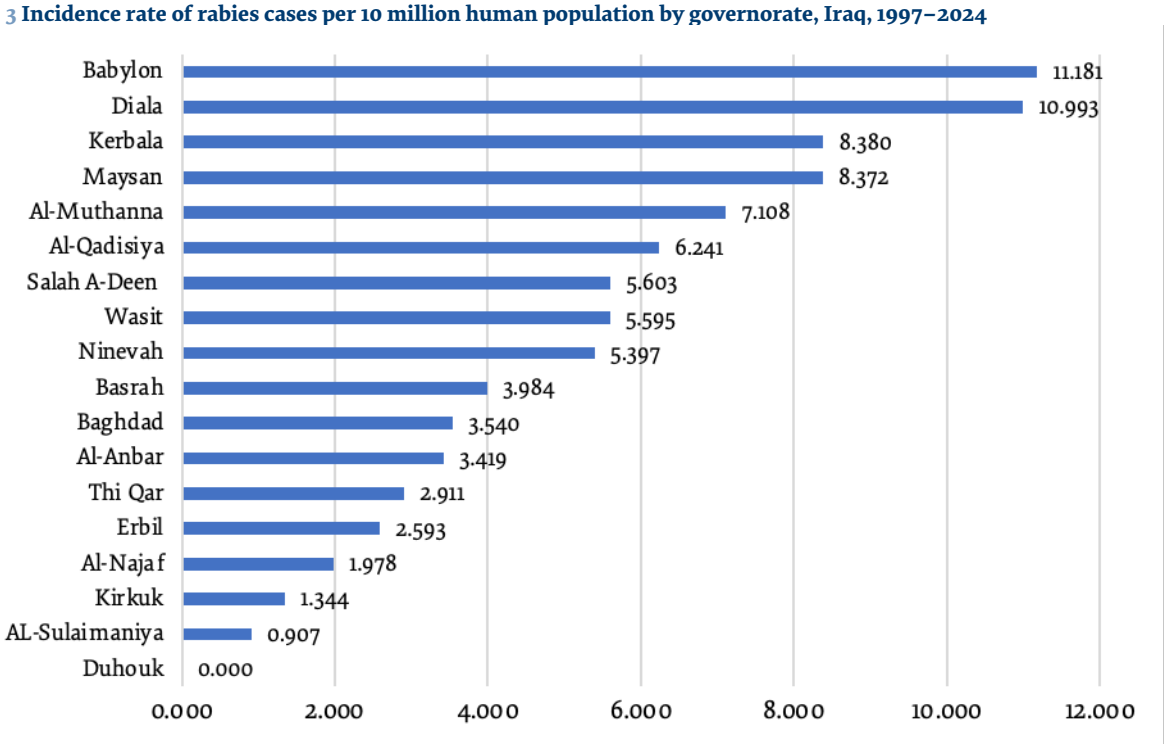


Table 1 Sociodemographic characteristics of reported rabies cases among humans, Iraq, 1997–2024

Percentage	No. of cases	Characteristic
Age group (years)		
60.2	263	<15
39.8	174	≥15
Sex		
82.2	359	Male
17.8	78	Female

in Asia and Africa, largely because of inadequate rabies control measures. India accounts for more than one third of global rabies cases, in which 2863 rabies cases were reported from India between 2005 and 2020. Rabies cases among humans continues to be reported in several countries of the Region, including Türkiye, Islamic Republic of Iran, Syrian Arab Republic, and Saudi Arabia (*10*,*11*).

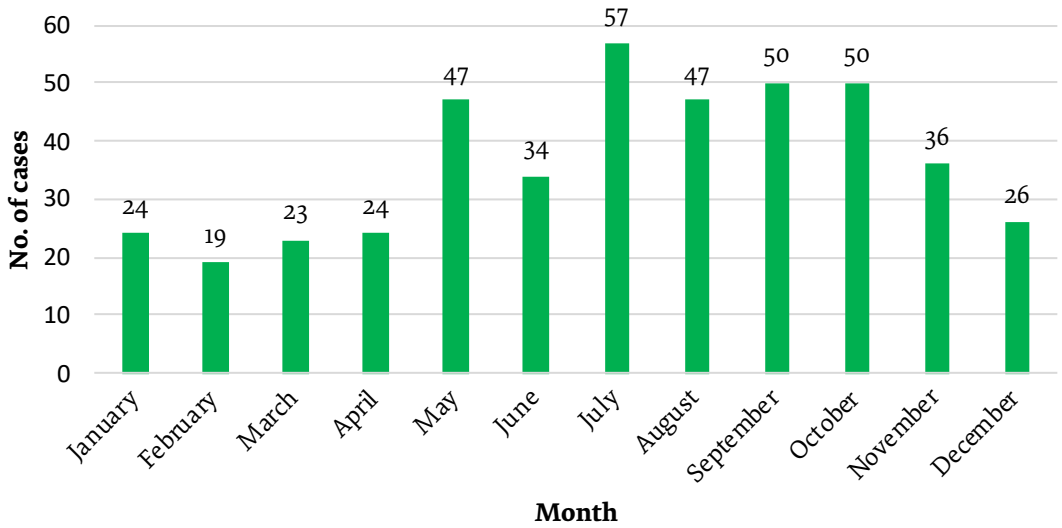
The number of rabies cases reported in Iraq was comparable to that reported in Morocco, where a mean of approximately 15 cases per year was documented between 2010 and 2017. In contrast, higher mean annual numbers of cases have been reported in Yemen (42 cases between 2011 and 2017) and Egypt (32.5 cases between 2010 and 2013). Lower mean annual numbers were reported in Bahrain between 2010 and 2017 (0 cases per year), Kuwait (0 cases per year, excluding 2014), Islamic Republic of Iran (5.9 cases per year), Syrian Arab Republic (3.6 cases per year) and Sudan (3.1 cases per year) (*5*,*12*).

In 2018, WHO launched a global strategic plan to eliminate rabies cases among humans by 2030 (*13*). However, Iraq remains far from achieving this target. Several factors may contribute to this situation, including limited surveillance of rabies among animals, insufficient dog vaccination and sterilization programmes, reliance on culling as a control strategy, limited understanding of the role of wildlife in the maintenance and transmission, intermittent shortages of rabies vaccine and immunoglobulin, incomplete adherence to post-exposure prophylaxis, a steadily increasing stray dog population, and weak regional coordination (*14*). Year-to-year fluctuations in reported cases, particularly following the 2003 invasion and subsequent periods of internal conflict, may reflect disruptions in surveillance capacity and population displacement rather than true changes in disease incidence.

Rabies cases were reported in all Iraqi governorates except Duhok. This may reflect underreporting or surveillance limitations rather than true absence of the disease. The national incidence rate was 4.63 per 10 million population. Higher incidence rates were observed in central and southern governorates, including Babylon, Diyala, Kerbela, Maysan, Al-Muthana, and Qadisiya, while the lowest rates were reported in the northern governorates, particularly Duhok, Sulaimaniya and Kirkuk. These geographical differences may be influenced by variation in stray dog density, frequency of animal bites, population density, proportion of rural areas, rural-urban interaction, and disparities in reporting practices across governorates.

Most reported cases occurred among children aged < 15 years (60.2%) and the majority were males (82.2%). This finding is consistent with WHO estimates indicating that approximately 40% of rabies deaths occur among children aged < 15 years (*3*). Similar age and sex distributions have been reported in India, where 29.2% of cases occurred among children aged < 15 years and 83.3% among males,

Figure 4 Monthly distribution of reported rabies cases among humans in Iraq, 1997–2024



as well as in other countries of the Region, where male predominance has been consistently observed (*15,16*). This may be related to greater outdoor exposure, especially in rural, poorer, and densely populated urban areas. The higher proportion of cases among children observed in Iraq may also be influenced by the relatively young age structure of the population.

Rabies cases were reported throughout the year, with a relative increase during summer and autumn months (May to October). This seasonal pattern may be related to the increased outdoor activity during school holidays, particularly among children, as well as greater exposure because of light clothing during warmer months. Comparable seasonal peaks have been reported in China, with increased incidence observed from June to November in one study period and from August to October in another (*17,18*).

Strengths and limitations of the study

A major strength of this study is the use of data from the national rabies surveillance system, the only source of nationwide information on rabies cases among humans in Iraq. This enabled inclusion of cases from all governorates and assessment of long-term temporal, geographical, and seasonal patterns. To our knowledge, this study provides the first comprehensive description of the epidemiology of reported rabies cases among humans in Iraq over nearly 3 decades.

This study has several limitations related to the use of routine surveillance data. Rabies case classification relied on clinical and epidemiological criteria, as laboratory confirmation before death is not routinely available and postmortem confirmation is not permitted. Inclusion of probable cases may therefore have led to underestimation or overestimation of the true incidence of rabies cases among humans. Some data were missing over the study period, particularly during periods of conflict, which may have affected reporting completeness.

Limitations also arise from the scope of information captured by the surveillance system. Earlier versions recorded only basic sociodemographic variables, such as age and sex, and did not include information on residence, occupation, or other factors influencing exposure risk. The private health sector is not formally integrated into the national rabies reporting system. Although most suspected cases are likely to present to public hospitals because of the severity of the disease, underreporting cannot be excluded. Information on knowledge, attitudes, and cultural beliefs related to rabies, as well as socioeconomic conditions, access to health care services, landscape characteristics, and proximity to transportation networks, was not available and could not be assessed. These contextual factors may have influenced reporting and prevention patterns across governorates.

Conclusion

This study documented 437 reported rabies cases among humans between 1997 and 2024, confirming that rabies remains a public health problem. Higher incidence rates were observed in several central and southern governorates, particularly Babylon and Diyala. Most cases occurred among children aged <15 years and males, and cases were reported throughout the year, with a relative increase from May to October. These findings highlight the importance of strengthening rabies control measures in Iraq, including management of stray dog populations, expanded animal vaccination programmes, raising public awareness, and ensuring sustained availability of rabies vaccines and immunoglobulin. Implementation of these measures should take existing resource constraints into account.

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Impact of the COVID-19 pandemic on primary health care reform in Pakistan

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Abstract

Background: Primary health care reform in low- and middle-income countries involves complex processes of prioritisation and agenda-setting. Evidence remains limited on how the COVID-19 pandemic influenced these processes at the subnational level.

Aim: To examine how COVID-19 affected primary health care reform in Khyber Pakhtunkhwa, Pakistan.

Methods: We conducted semi-structured interviews with 14 key informants, including provincial health leaders, provincial political leaders and their advisers, and representatives of national and international organisations, and reviewed relevant supporting documents. We analysed the data inductively through thematic coding and process tracing across data sources.

Results: Most of the respondents agreed that the pandemic facilitated the implementation of reforms at the primary health care level, by strengthening advocacy and political influence. The reforms began around August 2020 and included improved financial management and allocation of resources, establishment of primary health care management committees, increased budget for essential medicines, recruitment of additional frontline clinical staff, and outsourcing of selected support services. Investments in public health increased through an almost 40% increase in the health budget between the 2019/2020 and 2022/2023 financial years.

Conclusion: COVID-19 created an opportunity to advance primary health care reform at the provincial level in Khyber Pakhtunkhwa, Pakistan. There is a need to sustain and improve on these reforms to strengthen primary health care services and advance towards the longer-term health goals and Universal Health Coverage.

Keywords: COVID-19, primary health care, health reform, health policy, UHC, Pakistan

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Background

Primary health care (PHC) is central to improving access to essential services and advancing progress towards Universal Health Coverage (*1–3*). The COVID-19 pandemic had a significant impact on health systems and may have accelerated changes in the organisation and functioning of PHC systems (*4–7*). While the long-term implications of COVID-19 for PHC remain uncertain, early stages of the policy process, namely reform prioritisation, are likely to reveal indirect effects of the pandemic.

Evidence on the impact of COVID-19 on PHC systems in low- and middle-income countries (LMICs) remains limited. Existing literature has largely focused on the immediate impact on service delivery during emergency response, or on selected priority areas such as childhood immunisation, maternal and child health care, and the scale-up of emergency services (*4,6–11*). Fewer studies have examined the indirect effects of the pandemic on health system reform processes, although emerging evidence from India suggests that COVID-19 influenced policy priorities beyond the acute response phase (*12*).

Policy process theory offers analytical tools for examining how reform priorities emerge and change. Kingdon's Multiple Streams Framework (MSF) is widely applied in policy analysis and conceptualises agenda-setting as the convergence of problem, policy and political streams, often triggered by a focusing event that opens a policy window (*13*). Large-scale shocks may alter perceptions of health system performance or political feasibility, thereby creating opportunities for reform. The COVID-19 pandemic may therefore have functioned as a focusing event, reshaping primary health care reform priorities within different institutional and governance contexts.

Path dependency further highlights how past policy decisions shape subsequent reform trajectories. Policy Feedback Theory (PFT) applies this concept to explain how existing policies influence political dynamics and future change (*14,15*). However, path dependency has rarely been integrated explicitly into MSF-based analyses. An exception is a modified MSF incorporating PFT and path dependency, developed by Spohr and applied in analyses of European labour market policies (*16*). This integrated

perspective highlights how reform priorities may shift following a major health system shock.

In Pakistan, a lower-middle-income country with a Gross Domestic Product of US$1597 per capita, such shifts occurred in the context of PHC reform during the COVID-19 pandemic (*17*). Before that, the leading causes of mortality included neonatal conditions and non-communicable diseases (*18*). In 2021, COVID-19 became the leading cause of death (*19*). Khyber Pakhtunkhwa, the third largest province in Pakistan, has a population of 41 million and has experienced recurrent natural disasters and conflict, contributing to population displacement and increased communicable disease transmission (*20–22*). The provincial department of health comprises 887 basic health units (BHUs) and rural health centres (RHUs) delivering essential preventive and curative services (*23*). Key pre-pandemic reforms included the devolution of health system governance to the provincial level in 2010 and initiatives to outsource management of selected PHC facilities.

Pakistan's response to the COVID-19 pandemic has been described as relatively effective (*11,24,25*). In Khyber Pakhtunkhwa, a PHC reform agenda was developed in August 2020, following the initial emergency response. This case study examines how COVID-19 influenced PHC reform prioritisation in Khyber Pakhtunkhwa by comparing pre-pandemic and post-emergency reform agendas and analysing the drivers shaping reform decisions within a devolved health system.

Methods

Study design

This study used a qualitative case study design. Data were derived from semi-structured interviews with key informants and complemented by analysis of supporting documents using a clear audit trail. A narrow definition of PHC was applied, focusing on public sector formal health facilities providing first contact health care, including BHUs and RHUs (*26*).

Semi-structured interviews

Fourteen interview participants were identified through stratified purposive sampling (Table 1). Stakeholders included provincial department of health leaders, members of provincial political leadership and their advisers, and representatives of national and international organisations. Sampling aimed to achieve saturation among decision-makers directly involved in steering the provincial COVID-19 response. Saturation was considered reached when interview data became repetitive and no substantively new themes emerged. This assessment was confirmed through iterative review among the co-authors.

Table 1 Characteristics of semistructured interview participants

No.	Date and location of interview	Role	Organisation type	Engagement in COVID-19 response
1	December 2022, Peshawar, Pakistan	Director	Provincial government	Led COVID-19 response for the department of health at district level, later appointed at director level during pandemic; involved in PHC reform design
2	December 2022, Peshawar, Pakistan	Director	Provincial government	Member of the team leading the COVID-19 response at provincial level; involved in PHC reform design
3	December 2022, Peshawar, Pakistan	Executive Director	Provincial government	Led the department of health response during part of the COVID-19 pandemic; involved in PHC reform design
4	December 2022, Peshawar, Pakistan	Deputy Director	Provincial government	Member of the team leading the COVID-19 response at provincial level; involved in PHC reform design
5	December 2022, Peshawar, Pakistan	Director	Provincial government	Member of the team leading the COVID-19 response at provincial level
6	December 2022, Peshawar, Pakistan	Leader	Provincial government	Political leader responsible for the COVID-19 response within the provincial government
7	December 2022, Peshawar, Pakistan	Adviser	Provincial government	Adviser to political leadership for the COVID-19 response at provincial level
8	December 2022, Peshawar, Pakistan	Director	Provincial government	Led the COVID-19 response for the department of health at district level
9	December 2022, remote (video call)	Executive Director	Provincial government	Led department of health response during part of the COVID-19 pandemic, involved in PHC reform design
10	December 2022, remote (video call)	Adviser	Provincial government	Adviser to political leadership for the COVID-19 response within the provincial government
11	March 2023, remote (video call)	Adviser	International organisation	Adviser to provincial government COVID-19 response
12	March 2023, remote (video call)	Adviser	International organisation	Adviser to provincial government COVID-19 response
13	March 2023, remote (video call)	Adviser	National organisation	Adviser to provincial government COVID-19 response and PHC reform design
14	April 2023, remote (video call)	Adviser	International organisation	Consultant supporting PHC reform design

Interviews were conducted in person or remotely through video calls between December 2022 and April 2023 by the lead author. A second author independently reviewed 2 interview transcripts to ensure consistency of coding and interpretation.

Review of supporting documents

Supporting documents were identified through recommendations from interview participants, complemented by a search of publicly available sources. In total, 9 documents were reviewed, including 5 non-public documents provided by interview participants and 4 documents in the public domain. Document analysis was conducted using a process tracing approach, with data extracted using the READ (Read, Extract, Analyse, Distil) framework, aligned with the temporal focus of the research questions (*27*,*28*).

Data analysis

Interview transcripts and supporting documents were coded to inform the development of analytic memos for each interview. Inductive thematic coding of health system-related themes was conducted by the lead author using ATLAS.ti (*29*). Memos prepared in Microsoft Word were combined with field notes and data extracted from document analysis to identify recurrent patterns and potential causal mechanisms (*30*). These were iteratively examined and refined through subsequent interviews using an explaining-outcome process tracing approach to assess causal pathways.

Results

Pre-COVID-19 and early COVID-19 priorities

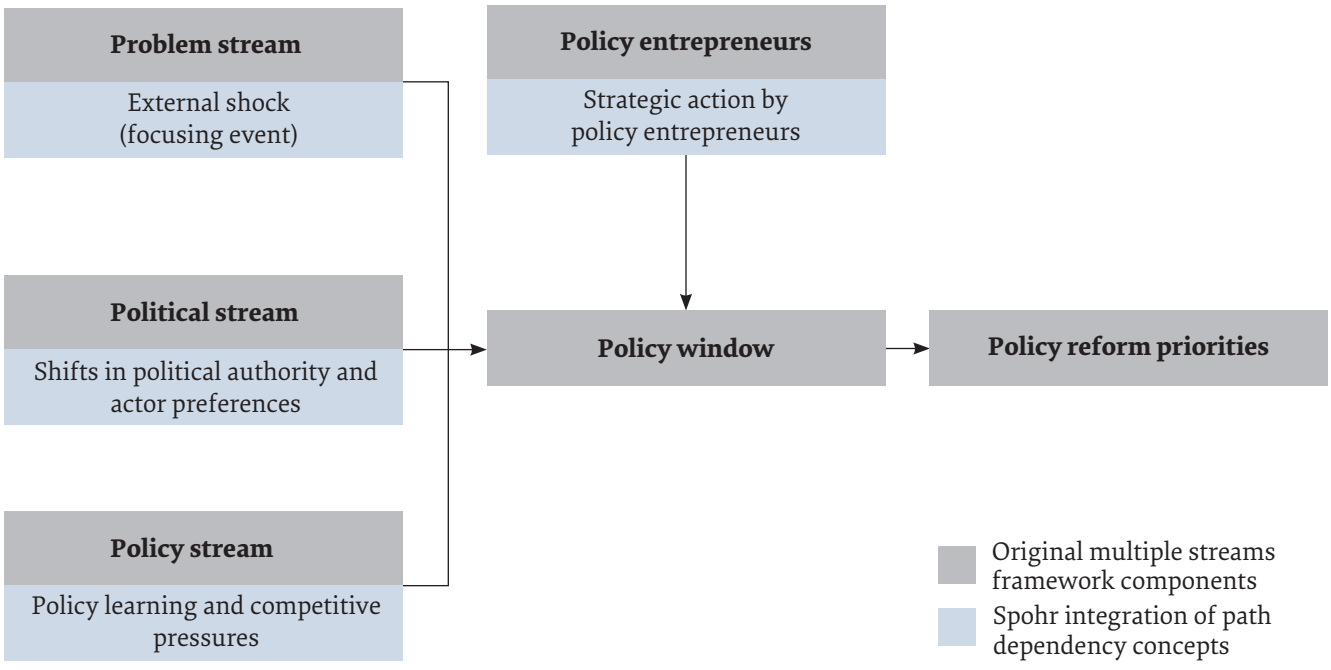
Interview participants with technical backgrounds said that pre-COVID-19 priorities were largely driven by external influences and reactive agenda-setting. These included donor priorities linked to international commitments and heightened public attention following negative media coverage, such as localised outbreaks of dengue fever (*31*). One respondent said:

> *"TB and HIV are global commitments, and the Global Fund puts its resources there. To match those resources, the provincial government is compelled to invest as well."* (Provincial department of health official)

Participants with political backgrounds described a different set of priorities, focusing on the construction of new health facilities, often within the constituencies of influential politicians, and the expansion of human resources. Across both technical and political groups, pre-COVID-19 priorities were shaped by 3 dominant factors: donor and international expectations, negative media coverage, and perceptions of voter preferences (Figure 2).

The early COVID-19 emergency response from March 2020 to August 2020 prioritised hospital-based and public health interventions. During this period, the PHC system played 2 main roles. First, it served as a source of human resources, with PHC doctors seconded to hospitals that were rapidly expanded to manage early COVID-19 waves. Second, PHC staff supported rapid response teams involved in COVID-19 track-and-trace activities in Khyber Pakhtunkhwa.

Figure 1 Conceptual framework integrating the multiple streams framework with temporal and path-dependent elements (*16*)



Emergence of new primary health care reform priorities

The main priorities of the PHC reform agenda developed around August 2020 focused on areas requiring additional financial allocation. These included devolving aspects of financial management to BHUs and RHCs through the establishment of PHC management committees, increased budget for essential medicines, recruitment of additional frontline clinical staff through contract arrangements, and outsourcing of selected support services.

Interview respondents described changes in performance management practices, including more frequent operational and performance review meetings led by senior department of health officials and supported by digital communication and data systems (Figure 2).

Although participants reported that many reform ideas pre-dated COVID-19, views differed on whether the pandemic itself constituted a focusing event. However, there was broad agreement that the pandemic facilitated the implementation of the reform agenda by increasing urgency, addressing performance gaps, strengthening the political influence of reform advocates, and allowing reforms to be tested during the emergency response (Figure 2).

Participants reported that reform discussions fluctuated with the rise and fall of COVID-19 cases. One respondent said:

> *"Whenever the wave was rising, nothing else was discussed. Whenever the number of cases decreased, there was a discussion about potential areas of primary and secondary health care reform, not from the COVID learning or compliance, but from a general desire of the provincial government to improve primary and secondary health care."* (Provincial political adviser)

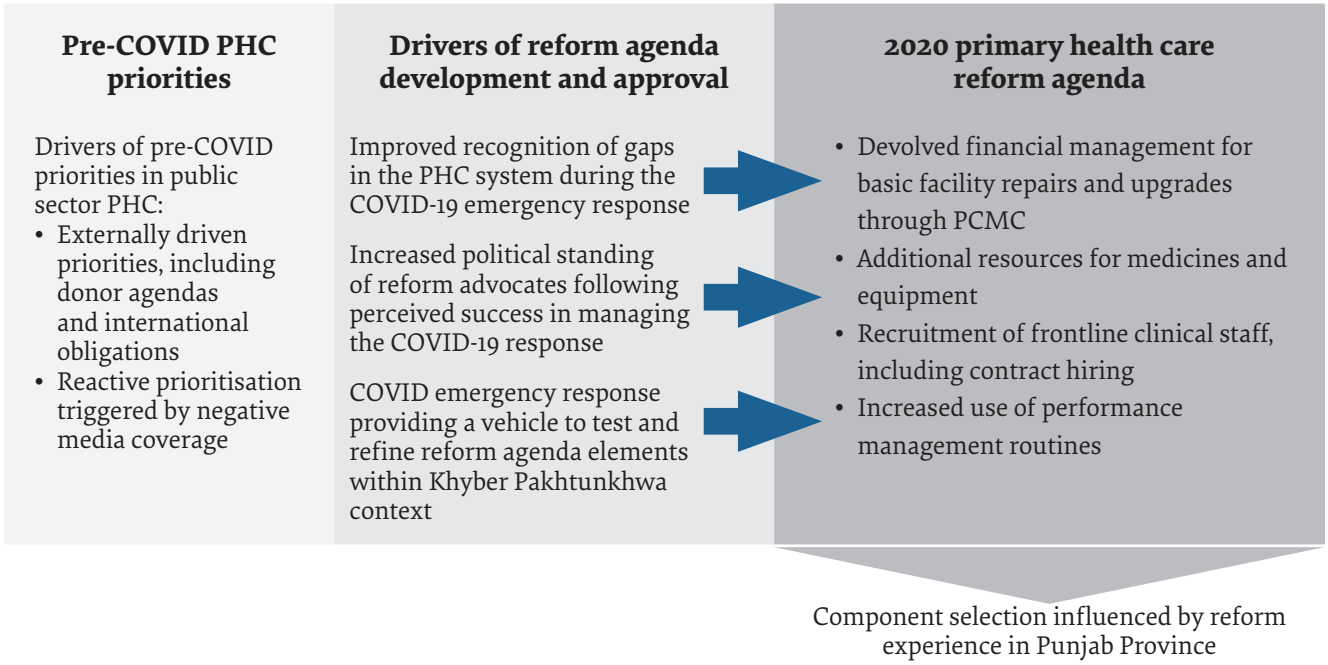
Most participants identified neighbouring Punjab Province as a key source of reform ideas, reflecting reforms implemented there from 2016. Participants also linked COVID-19 experiences to the feasibility of reform implementation in Khyber Pakhtunkhwa. For example, financial devolution to hospitals during the early emergency response, combined with experience from the medical teaching institution initiative at the tertiary level, informed reform design at the PHC level. COVID-19 was also described as having exposed system weaknesses and increased urgency for reform. A provincial department of health official said:

> *"COVID showed us where the health system was weak".* (Provincial department of health official)

Early implementation of the reform agenda included the transfer of more than 600 million Pakistani Rupees (approximately US$ 3 million at the time) to PHC management committees for facility improvements in 550 BHUs by mid-2022, and the recruitment of more than 120 medical officers under contract. A considerable increase in public health investments was observed, with the overall health budget increasing by almost 40% between the 2019/2020 and 2022/2023 financial years (*23*). Respondents attributed this increase to the alignment of health and finance leadership roles and to heightened political support for health spending following COVID-19.

> *"[It is] true that, after COVID, [the] importance of investing in health has increased even further because people saw its effects directly."* (Provincial political adviser)

Figure 2 Pre-COVID-19 priorities, drivers of primary health care reform, and reform agenda components



Participants further noted that the reform momentum was strengthened by the increased political influence of health reform and by positive experiences that demonstrated the feasibility and effectiveness of interventions during the emergency response. One respondent said:

> *"(the Minister of Health) would not have had the leadership time to focus on these issues, if it were not for the pandemic".* (International organisation adviser)

Future of primary health care reforms

Interview participants were generally optimistic about the sustainability of reforms, particularly those related to financial devolution, human resources and medicines. However, political participants expressed concern about the continuity of reforms if senior leadership changed.

In January 2023, the provincial government was dissolved due to broader political developments, resulting in changes in senior health leadership under a caretaker administration (32). Interviews conducted in early 2023 highlighted concerns that leadership turnover and fiscal pressures could undermine the 2020 reform efforts. Participants identified protective factors, including the continued presence of technical leaders involved in reform design and the difficulty of reversing reforms that were already contractually or financially committed. At the same time, several participants with a technical background expressed concern that emphasis on visible facility-based investments, reinforced during the COVID-19 period, had reduced attention to preventive and long-term primary health care functions. One participant described how electoral incentives shaped political priorities:

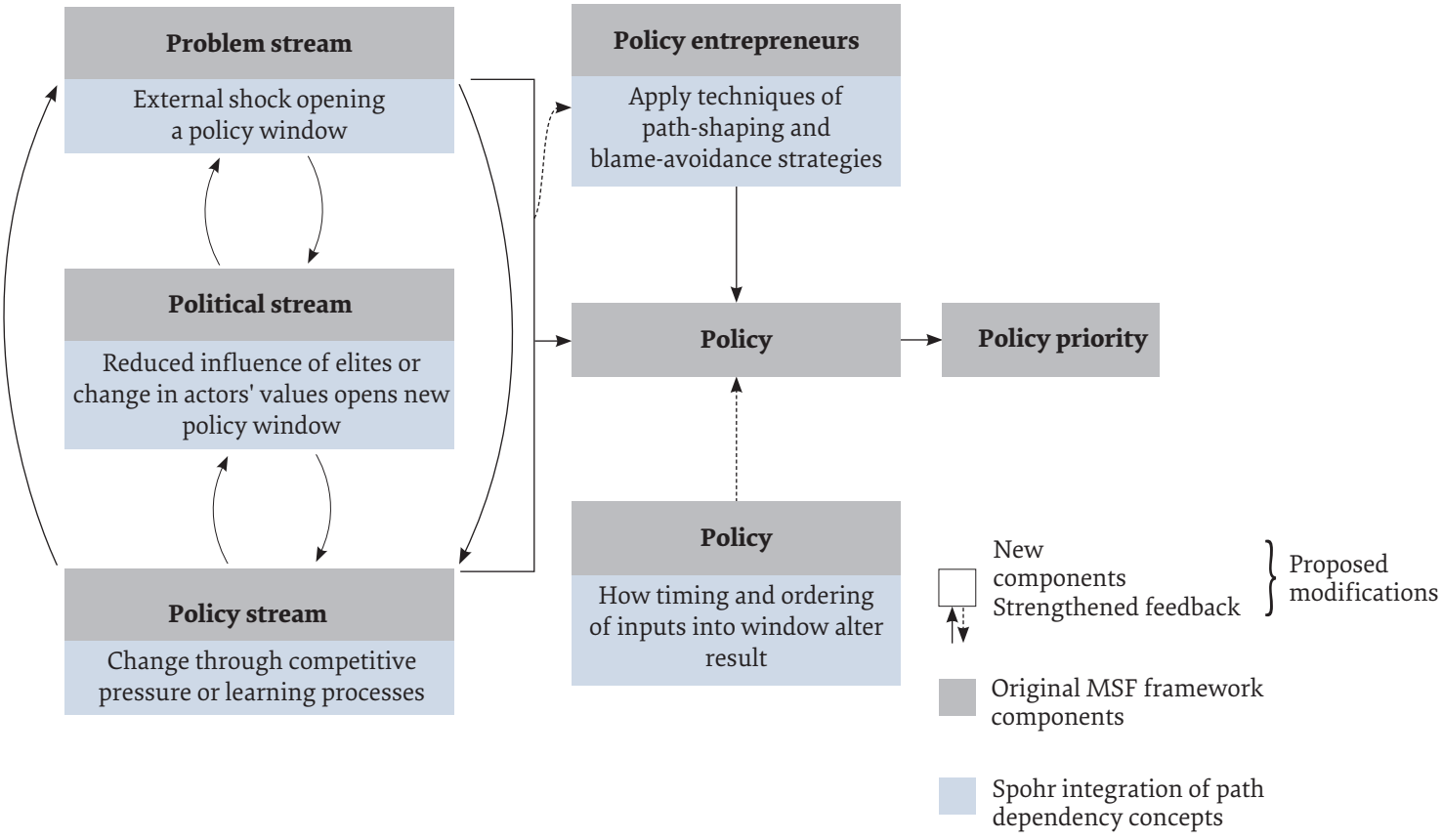
> *"Political leadership follows public demand. When they go in their constituency, people complain about the lack of doctors and medicines. No one asks about vaccination, antenatal care, nutritional services, surveillance of epidemic diseases, or vaccination for preventable diseases."* (Provincial department of health official)

Refinements to the modified multiple streams framework integrating policy feedback theory

Accounts of the participants suggested that COVID-19 influenced all 3 MSF streams (Figures 2 and 3). Shared recognition of gaps in the health system shaped the problem stream, while the perceived success of the COVID-19 response strengthened political authority and resource mobilisation within the health sector. The policy stream was affected by the reform experience in Punjab Province and by the leadership interest in pursuing a legacy reform.

The mechanics driving the reform effort in Khyber Pakhtunkhwa during the COVID-19 pandemic aligned closely with the modified MSF based on the framework by Spohr. However, the analysis suggests several refinements that could increase the framework's utility in describing the effects of COVID-19 and similar events

Figure 3 Proposed refinements to modified MSF integrating PFT for the Khyber Pakhtunkhwa case example



on health policy processes, as illustrated in a revised version of the framework (Figure 3).

The first refinement relates to the role of feedback loops between newly adopted policy agendas and components of the modified framework integrating PFT. This reflects the influence of previous policy decisions and the existing policy environment on the emergence of subsequent reform agendas (*14*). In Khyber Pakhtunkhwa, the successful adoption of new policies and allocation of resources to these policies created a positive feedback loop that supported later reform components (*33*).

The second refinement relates to the need to place greater emphasis on interactions between different components of the modified MSF. In Khyber Pakhtunkhwa, the 3 streams were influenced by a small policy community of fewer than 12 individuals. The MSF does not fully capture the interdependence of these components, as noted in previous analyses (*14*).

Third, greater attention should be given to the timing and sequencing of key factors within the MSF. In Khyber Pakhtunkhwa, a reform example from the neighbouring Punjab Province was presented at a time when a reform agenda was being explored. Had the timing differed, the resulting reform agenda may have taken a different path.

Discussion

This case study describes a pre-COVID-19 PHC system that was largely reactive and shaped by external influences. During the pandemic, the system evolved towards a reform agenda led by local health system actors and informed by experiences from neighbouring provinces and lessons emerging from the pandemic response.

Some findings from this study may be transferrable to other LMIC PHC systems with comparable characteristics, including large populations, performance gaps and decentralised governance structures (*1*). The findings highlight the role of a small and cohesive policy community in advancing a shared reform agenda and demonstrate pandemic-related shifts in political influence among actors engaged in the reform. Taken together, the findings suggest that the COVID-19 pandemic opened a time-limited window of opportunity for reform that was recognised and acted upon by policymakers. This window emerged through a heightened awareness of health system performance gaps, the availability of solutions tested during the early emergency response, and increased political standing of key reform advocates.

The modified MSF framework proved useful in understanding the drivers of the reform process observed in this case. Refinements that emphasise feedback cycles, strengthen interactions between streams and elevate the role of timing and sequencing may enhance the relevance of the framework for analysing health reforms in LMICs. We recommend the expanded use of this type of policy frameworks to support understanding of policy reform in health systems.

Despite the prominence of the reform agenda in provincial discourse on PHC, its long-term trajectory remains uncertain. The period following data collection was characterised by rapid political change and worsening fiscal pressures in Pakistan. Follow-up discussions with interview participants suggested that some reform components demonstrated continuity, while others experienced delays or setbacks in implementation, including additional budget allocations for medicines and contracting of human resources. Further research could expand on the paths these reforms followed after their initial implementation and the factors influencing their sustainability.

This study has several limitations. The sample comprised a small number of relatively senior key informants, many of whom were known to the lead author through previous engagement in the health policy context in Pakistan. This may have introduced social desirability or other response biases, and may have influenced the analysis through author positionality. The politically dynamic context in which the study was conducted, together with the time lag against which participants recalled events, may have contributed to recall bias and may limit the broader applicability of the findings.

Conclusion

The COVID-19 pandemic played a critical role in advancing a new PHC reform agenda in Khyber Pakhtunkhwa, Pakistan. This case study offers insights for national and global policymakers on recognising and acting upon policy windows to support broader systems reforms, using the interventions and policy processes mobilised during the pandemic to help advance longer-term goals related to PHC and universal health coverage. The proposed refinements to the modified MSF framework integrating PFT may enhance its usefulness for evaluating the effects of COVID-19 and other events focusing on policy processes in similar settings.

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Resurgence of measles in Bosnia and Herzegovina amid declining vaccination coverage

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Abstract

Background: Sarajevo Canton reported large measles outbreaks in 2019 and 2024, highlighting the impact of the persistent gaps in immunisation coverage.

Aim: To analyse 2 measles outbreaks in Sarajevo Canton in Bosnia and Herzegovina, identify populations at risk and assess the impact of vaccination coverage on disease transmission.

Methods: We collected publicly available weekly case counts data for 45 weeks from the Public Health Institute of Sarajevo Canton and examined the vaccination coverage for 5 years to assess the impact of immunisation on outbreak dynamics. We conducted descriptive analyses using RStudio version 2024 and evaluated the differences between outbreaks using Mann-Whitney U test. $P < 0.05$ was considered statistically significant.

Results: A total of 869 cases were reported in 2019 and 4505 in 2024, and children aged 1–4 years were mostly affected (42.1%). Most of the cases were either unvaccinated or had unknown vaccination status; 92.3% of cases in 2019 were unvaccinated, and 87.7% in 2024 were unvaccinated, while 9.9% had unknown vaccination status. The 2024 outbreak had a higher and longer peak (416 vs 91 cases) occurence than 2019, and one death was reported in each year.

Conclusion: The declining vaccination coverage in Sarajevo Canton contributed to increased measles incidence. Strengthening mandatory immunisation, targeted catch-up campaigns and public communication are essential to achieve herd immunity, prevent future outbreaks and progress towards Universal Health Coverage.

Keywords: measles, vaccination, immunisation, MMR vaccine, Sarajevo Canton, Bosnia and Herzegovina

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Introduction

Measles is a highly contagious viral disease that remains a major global public health threat. Despite the availability of an efficacious vaccine since the 1960s, outbreaks persist, particularly in areas with low vaccination coverage (1). Transmission occurs through respiratory droplets, and the high basic reproduction number of the virus (R_0) allows infection after brief exposure among unvaccinated individuals (2). Before widespread immunisation, measles was nearly universal during childhood, but mass vaccination programmes dramatically reduced incidence worldwide. However, vaccine hesitancy, barriers to health care access, and socioeconomic factors have contributed to renewed outbreaks in many regions (3). WHO prioritises measles elimination, emphasising the need to achieve and maintain vaccination coverage of at least 95% to ensure herd immunity (1).

In Sarajevo Canton, measles vaccination follows national regulations and the official immunisation calendar of the Public Health Institute of the Federation of Bosnia and Herzegovina (4,5). The measles–mumps–rubella (MMR) vaccine is mandatory for children aged 12 months to 14 years, with the first dose at 12 months and the second at 6 years. Children who miss scheduled doses may receive catch-up or early vaccination in high-risk situations (4).

In early 2024, 3 confirmed cases of measles were reported in Sarajevo Canton, marking the onset of a new outbreak following a previous outbreak in 2019 that persisted until August of that year.

This study analyses and compares the epidemiological characteristics of these 2 outbreaks in Canton Sarajevo and examines the relationship between vaccination coverage and disease spread.

Methods

Study design and data sources

This study analysed epidemiologic data from 2 measles outbreaks that occurred in Sarajevo Canton in 2019 and 2024. Aggregate surveillance data were obtained from routine reports of the Public Health Institute of Sarajevo Canton, while individual-level information on age, sex, and vaccination status was collected through standard epidemiologic questionnaires and review of medical records. Weekly case counts over a 45-week period were used to construct epidemiologic curves, and 5-year

vaccination coverage trends were examined to assess the impact of immunisation on outbreak dynamics.

Case definition

Cases were classified according to the European Centre for Disease Prevention and Control (ECDC) definitions as possible, probable, or confirmed (*6*). A possible case met clinical criteria (fever, rash, and either cough, coryza, or conjunctivitis). A probable case met clinical criteria with an epidemiologic link, while a confirmed case was not recently vaccinated and met both clinical and laboratory criteria.

Index cases in both outbreaks were confirmed using polymerase chain reaction (PCR). During the 2024 outbreak, 50 cases were confirmed using PCR and 11 cases using serology testing (IgM positive). The remaining cases were classified as probable based on clinical presentation and exposure links.

Surveillance and outbreak response

Surveillance activities included active case finding, contact tracing, and field investigations. Suspected cases were identified in primary and secondary health care settings through clinical diagnosis or laboratory confirmation. Parents were interviewed to collect information on symptoms, exposures, school or childcare attendance, and vaccination history. Household visits, institutional surveys, and further investigations (such as school records and travel history) were conducted to identify transmission chains and geographic clustering.

Outbreak control measures involved intensified case finding, isolation of cases, emergency vaccination clinics operating in 2 shifts across the canton, and targeted public communication campaigns. Priority was given to children under 6 years and school-aged children who were unvaccinated or partially vaccinated.

Statistical analysis

Descriptive analyses were conducted using RStudio (version 2024.12.0+467). Categorical variables, including age group, sex, and vaccination status, were summarised as frequencies and percentages, while continuous variables, such as patient age, were assessed for normality and reported as medians with interquartile ranges (IQR). Differences between outbreaks were evaluated using the Mann–Whitney U test, with a $P < 0.05$ considered statistically significant. Epidemic curves were generated by plotting weekly case counts over a 45-week period, and geographic distribution was illustrated by mapping case counts across municipalities. A 21-day moving average was applied to smooth short-term fluctuations, accounting for the measles incubation period and highlighting the overall epidemic trend.

Ethics considerations

Ethics approval was not required because the study used pseudonymised routine surveillance data collected for public health purposes.

Results

Overview of measles outbreaks

During the past decade, Sarajevo Canton experienced 3 measles outbreaks. The first occurred in 2014–2015, with 1251 cases. After sporadic cases in subsequent years, an outbreak in 2019 resulted in 869 cases between January and July. No cases were reported from 2020 to 2023, likely due to COVID-19 containment measures. A third outbreak started in February 2024, with 4505 reported cases by the end of the year. Transmission continued through 2024 (Figure 1).

Vaccination coverage

Declining vaccination coverage preceded each outbreak. Following the 2014 outbreak, a catch-up vaccination campaign increased coverage to 91.0% for the first MMR dose and 97.0% for 2 doses. Coverage subsequently decreased sharply, reaching 63.4% for 2 doses in 2015, amid growing vaccine hesitancy. During the 2019 outbreak, catch-up activities failed to achieve adequate uptake, with only 44.7% of the target population receiving 2 doses.

In 2020, pandemic-related restrictions temporarily halted routine immunisation services for approximately 2 months, further reducing coverage. By the end of the year, only 32.4% of the target population had received one MMR dose and 24.1% had received 2 doses (Figure 1). Despite renewed vaccination efforts in subsequent years, uptake remained limited.

In early 2024, intensified campaigns were implemented, including walk-in vaccination services and direct outreach to parents. Enforcement measures, including penalties for vaccine refusal, were also applied, resulting in improved coverage (63.2% for the first dose, and 46.9% for 2 doses) by the end of the year.

Characteristics of cases

In both outbreaks, children aged 1–5 years were most affected (Table 1). Sex distribution did not differ significantly between years ($P = 0.232$). Median age increased from 5 years (IQR 2–18) in 2019 to 7 years (IQR 3–12) in 2024 ($P < 0.001$).

Most patients were either unvaccinated or had unknown vaccination status. In 2019, 92.3% were unvaccinated or undocumented, 2.9% had received one MMR dose, and 4.8% were fully vaccinated. In 2024, 87.7% of cases were unvaccinated and 9.9% had unknown vaccination status, mainly among adults with missing immunisation records, together accounting for 97.7% of cases. Only 1.6% had received one dose, and 0.7% were fully vaccinated.

Epidemic curves

Both outbreaks showed rapid increase in cases between epidemiologic weeks 6 and 11 (Figure 2). However, the 2024 outbreak continued to intensify for an additional 6 weeks, peaking at 416 cases in week 16, compared with a

Figure 1 Measles cases and MMR vaccination coverage in Sarajevo Canton, 2014–2024 (1a. Number of reported measles cases over a 10-year period. 1b. MMR vaccination coverage trends over the same period)

Figure 1a

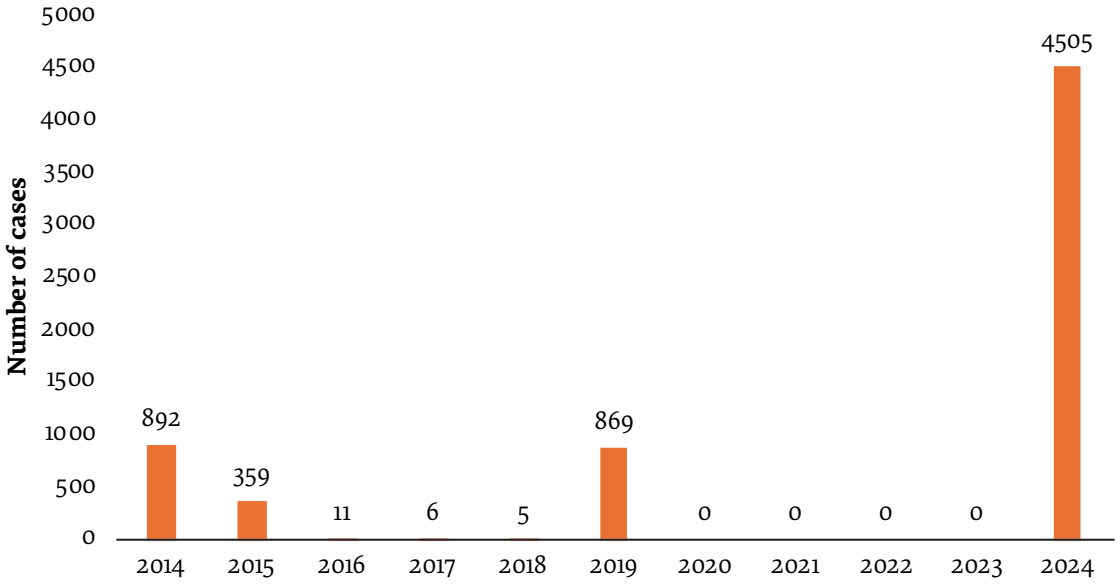
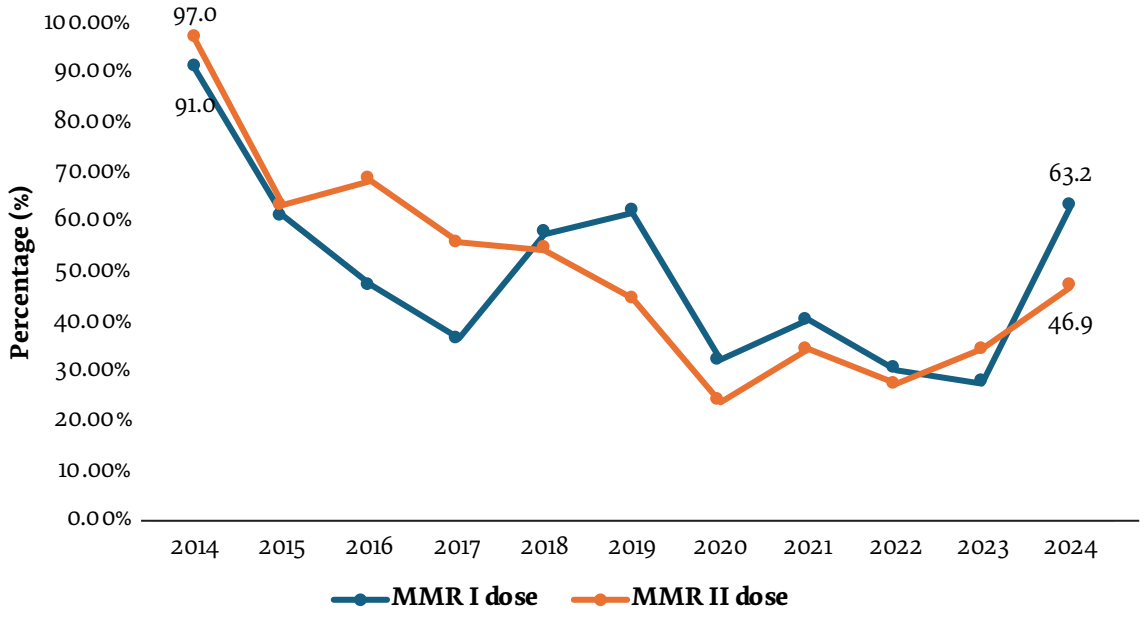


Figure 1b



peak of 91 cases in week 11 of 2019. Each outbreak resulted in one death.

Discussion

Analysis of the 2 recent measles outbreaks in Sarajevo Canton highlights a concerning and consistent pattern of increasing case numbers associated with decreasing vaccination coverage. The proportion of unvaccinated individuals increased from 92.3% in 2019 to 97.7% in 2024, coinciding with an approximately 5-fold increase in reported cases. Given the ≥ 95% coverage required for herd immunity, both outbreaks illustrate how even modest declines in uptake can sustain widespread transmission.

Childhood vaccination coverage in Bosnia and Herzegovina has been decreasing steadily since 2014 (7). Although MMR first dose coverage showed a modest

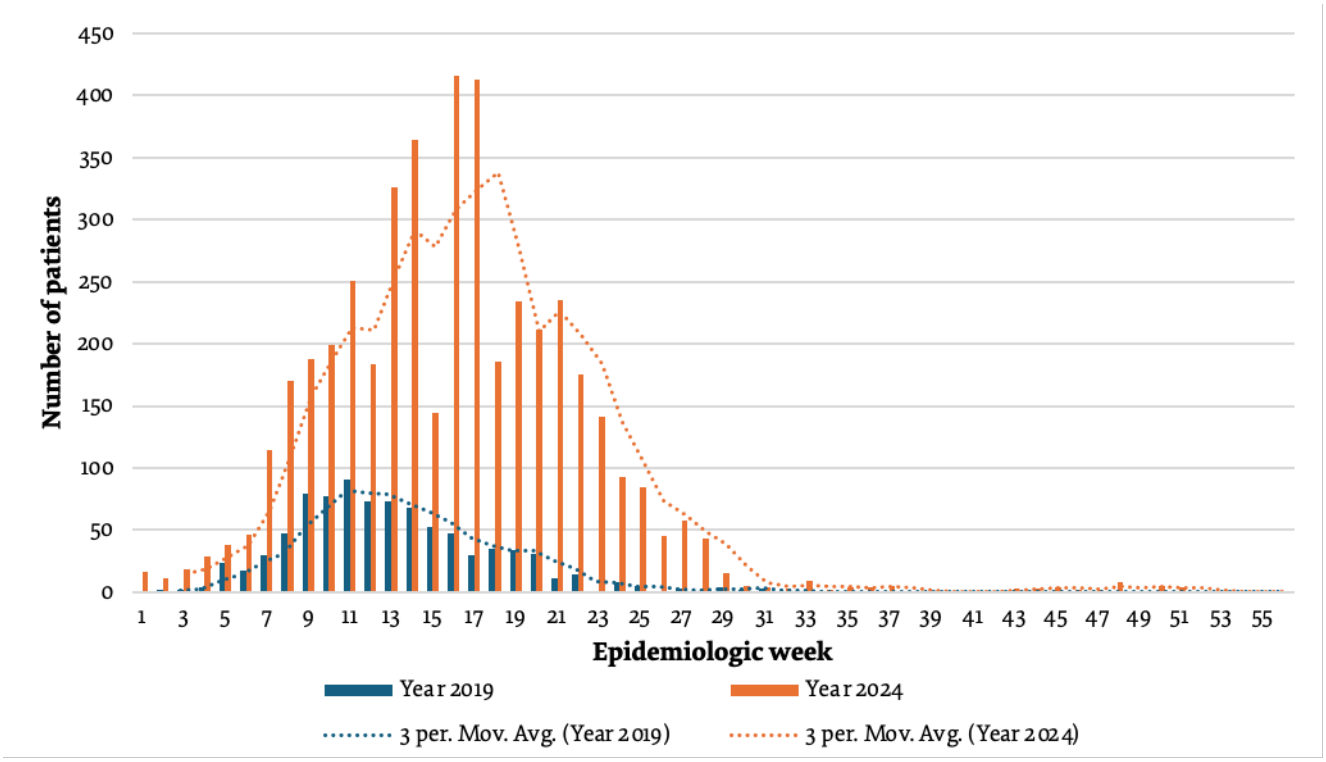
Table 1 Demographic characteristics and vaccination outcomes of measles cases in Sarajevo Canton, 2014–2024

	2019		2024	
Sex	**N**	**%**	**N**	**%**
Male	431	49.6	2334	51.8
Female	438	50.4	2171	48.2
Age (median and IQR)	5 (2–18)		7 (3–12)	
Age groups (years)	**N**	**%**	**N**	**%**
< 1	19	2.2	187	4.2
1–4	366	42.1	1549	34.4
5–9	189	21.8	1307	29.0
10–14	61	7.0	631	14.0
15–19	24	2.7	133	3.0
20–29	60	6.8	234	5.2
30–65	150	17.3	462	10.3
≥66	0	0.0	2	0.04
Deaths	1	0.12	1	0.02

improvement in 2019 (79.0%), it remained substantially below the threshold required for measles elimination (*8,9*). Weak enforcement of mandatory immunisation policies, inconsistent reporting of parental refusal, and increased vaccine hesitancy contributed to this outcome. These challenges were further exacerbated during the COVID-19 pandemic, when routine immunisation services were disrupted, resulting in a 26.7% reduction in coverage in 2020 (*7*).

The clinical and public health impact of these outbreaks was substantial. During late 2023 and early 2024, clusters of hospitalised measles cases were reported among preschoolers, most of whom were unvaccinated (*10*). Similarly, a 2024 study conducted at the University Clinical Centre of Sarajevo identified 279 laboratory-confirmed cases with complications such as pneumonia and otitis media, as well as severe neurologic outcomes, including meningoencephalitis and transverse myelitis. Two fatal cases were reported, both among unvaccinated children with underlying comorbidities (*11*). These findings are consistent with observations from the 2019 outbreak in Bosnia and Herzegovina, during which most cases occurred among unvaccinated children

Figure 2 Epidemic curves of measles outbreaks in Sarajevo Canton (2019 and 2024)



under 6 years of age, with measles virus genotype B3 predominating (12).

Regional comparisons with neighbouring countries reveal persistent regional disparities. While Croatia, Slovenia, and Serbia succeeded in maintaining high vaccination coverage after 2015, Bosnia and Herzegovina and North Macedonia experienced sharp declines, leaving substantial immunity gaps among their populations (13). WHO surveillance data confirm that Bosnia and Herzegovina and Serbia continue to rank among the countries with the lowest MMR coverage in Eastern Europe (14). Similar trends have been observed in Bulgaria, Montenegro, and Romania (15).

These patterns reflect broader global concerns about measles resurgence. In 2023, measles cases increased by 20%, with 10.3 million infections reported worldwide. More than 22 million children missed their first MMR dose, while second-dose coverage decreased to 74.0% (15). Within the WHO European Region alone, over 56 000 cases were reported during the first quarter of 2024 (16). Data from the European Centre for Disease Prevention and Control indicate a significant increase in measles cases across the European Union/European Economic Area in 2024, particularly in Romania, Italy, Germany, Belgium and Austria. Romania was among the most affected, reporting 27 568 cases and 18 deaths (17). These findings indicate persistent immunity gaps among children, adolescents and adults throughout Europe.

Public health implications

In the aftermath of the recent outbreaks, strengthening routine immunisation coverage, particularly ensuring timely completion of the 2-dose MMR schedule before school entry, remains the foremost priority. Sustainable preparedness requires robust surveillance systems, rapid outbreak response capacity, and closer integration with the education sector to promote vaccination awareness and school-based interventions. Strict protocols for case isolation and criteria for re-entry into educational settings should continue to be enforced.

Meaningful community engagement, targeted risk communication, and continuous monitoring and evaluation are essential to address vaccine hesitancy, assess intervention effectiveness and prevent future outbreaks. These findings support the need for urgent and coordinated action, including expanded vaccination campaigns, stronger enforcement of mandatory immunisation policies, and sustained investment in surveillance and outbreak preparedness.

Without decisive efforts to improve vaccination coverage, future measles outbreaks will likely result in increased morbidity, additional strain on healthcare systems, and heightened risk for vulnerable populations.

The 2 recent measles epidemics in Sarajevo Canton provide a clear illustration of the consequences of decreasing vaccine coverage. The remarkable increase in case numbers, together with the increasing proportion of unvaccinated individuals, indicate the cumulative risk posed by insufficient immunisation. Strengthening immunisation programmes and enforcing mandatory vaccination policies are essential to achieve herd immunity and prevent future outbreaks.

Study limitations

This study relied on routine surveillance data, which may underestimate case numbers due to underreporting, particularly in rural areas, or incomplete laboratory confirmation. Vaccination status was missing for some adults and data on hospitalisations were unavailable. Due to resource constraints, PCR or serological testing was not universally applied.

Conclusion

The 2019 and 2024 measles outbreaks in Sarajevo Canton highlight the critical impact of insufficient vaccination coverage. Sustained investment in immunisation programmes, surveillance, and public engagement is required to achieve herd immunity and prevent future outbreaks.

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Conflict of interests: None declared.

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Scaling up human papilloma virus vaccination in Pakistan

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Dear Editor,

Cervical cancer is the third most prevalent cancer among women in Pakistan, with over 5000 new cases and nearly 3200 deaths annually (*1*), yet our national response to human papilloma virus (HPV) prevention has been alarmingly slow. There is a strong link between persistent HPV infection and cervical cancer, and research studies have shown that HPV vaccines are safe and effective for preventing HPV-related diseases (*2*).

Recently, Pakistan took a crucial first step by launching its first HPV vaccination drive, which aims to immunise 13 million girls and train nearly 49 000 health workers to ensure smooth implementation (*3*). Encouragingly, the 12-day introductory campaign in September 2025 reached over 9 million girls across Punjab, Sindh, Azad Jammu and Kashmir (AJK), and Islamabad. Despite initial resistance fuelled by misinformation and social media rumours, trust-building efforts through community engagement, religious endorsements and visible government advocacy significantly improved acceptance. The health minister publicly vaccinated his own daughter during the campaign. National coverage exceeded 70%, indicating that with persistence and clear communication, parental hesitancy can be overcome (*4*).

To sustain this momentum, the initiative must be expanded beyond major cities into rural and underserved communities, ensuring inclusion of out-of-school girls and marginalised populations. High-coverage, school-based national HPV vaccination programmes have catalysed significant reductions in infection and disease burden in countries like Rwanda and Bhutan (*5*). These successful models in low- and middle-income countries provide strong and compelling proof of the efficacy and scalability of the vaccine.

The nationwide campaign marks an encouraging start, however, sustaining progress will require continued efforts to address cultural and social barriers against vaccination. Vaccine uptake remains hindered by misconceptions, particularly the belief that HPV vaccination encourages promiscuity. Reframing the vaccine as a tool for cancer prevention rather than, or in addition to, the prevention of sexually transmitted infections can help counter such myths. Equally important are sustained awareness drives and accessible screening programmes to ensure that the gains from this initiative translate into long-term cervical cancer prevention across Pakistan (*6*).

Policymakers, medical experts and the civil society should unite and prioritise HPV vaccination. The cost of inaction is reflected not only in numbers, but also in women who lose their lives to a disease that is largely preventable.

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