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## Prevalence and Case Fatality Rate of Antimicrobial Resistance Among Paediatric In-patients with ESKAPE Infections Aged 12 Years and Below at Kenyatta National Hospital, 2019-2022

### *Prévalence et taux de létalité de la résistance aux antimicrobiens chez les patients pédiatriques hospitalisés âgés de 12 ans et moins atteints d'infections ESKAPE à l'hôpital national Kenyatta, 2019-2022*

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#### ABSTRACT

##### Background

Antimicrobial Resistance (AMR) is a growing global health threat, especially with high-priority ESKAPE infections (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp.). Children are particularly vulnerable to the impact of resistant bacteria. Data on the current trends in prevalence and mortality of AMR in ESKAPE infections could prove invaluable in surveillance and management strategies.

##### Objective

To determine the prevalence and the case fatality rate of AMR in ESKAPE infections among children aged 12 years and below admitted to the paediatric ward in Kenyatta National Hospital (KNH) from June 2019 to June 2022.

##### Materials and Methods

A retrospective cross-sectional study design was conducted at KNH, involving paediatric inpatients aged 12yrs and below from June 2019 to June 2022 with ESKAPE infections. Simple random sampling technique was used and data was abstracted manually from KNH microbiology laboratory records and KNH health information records. Data was analysed using descriptive statistics.

##### Results

The overall prevalence of AMR was 35.3%. Enterobacter species accounted for 26.7%, Enterococcus faecium 11.1%, Staphylococcus aureus 19.1 %, Pseudomonas aureguinosa 8.3%, Klebsiella spp. 18.9%, and A. baumannii 15.9%. The median duration of in-hospital stay was 29 days, while the mean was 45 days. The mortality rate in AMR was 8.6% (12). Those aged below 6 years accounted for 58.3% of the deaths. Of those who died, girls accounted for 66.7%, and those with caregiver unemployment 66.7%.

##### Conclusion

More than 1/3 of children with ESKAPE infections had AMR (35.3%). With the mortality rate being as high as 8.6%, these statistics translate to a significant burden of mortality and prevalence in the context of the population as a whole.

**KEYWORDS:** ESKAPE, AMR, Prevalence, Case Fatality, Antibiotics

## RÉSUMÉ

La résistance aux antimicrobiens (RAM) constitue une menace sanitaire mondiale croissante, en particulier dans le cas des infections ESKAPE hautement prioritaires (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* et *Enterobacter* spp.). Les enfants sont particulièrement vulnérables à l'impact des bactéries résistantes. Les données sur les tendances actuelles en matière de prévalence et de mortalité liées à la RAM dans les infections ESKAPE pourraient s'avérer précieuses pour les stratégies de surveillance et de gestion.

### Objectif

Déterminer la prévalence et le taux de létalité de la RAM dans les infections ESKAPE chez les enfants âgés de 12 ans et moins admis dans le service pédiatrique de l'hôpital national Kenyatta (KNH) entre juin 2019 et juin 2022.

### Matériels et méthodes

Une étude transversale rétrospective a été menée au KNH auprès d'enfants hospitalisés âgés de 12 ans et moins entre juin 2019 et juin 2022 et atteints d'infections ESKAPE. Une technique d'échantillonnage aléatoire simple a été utilisée et les données ont été extraites manuellement des registres du laboratoire de microbiologie du KNH et des dossiers médicaux du KNH. Les données ont été analysées à l'aide de statistiques descriptives.

### Résultats

La prévalence globale de la RAM était de 35,3 %. Les espèces *Enterobacter* représentaient 26,7 %, *Enterococcus faecium* 11,1 %, *Staphylococcus aureus* 19,1 %, *Pseudomonas aeruginosa* 8,3 %, *Klebsiella* spp. 18,9 % et *A. baumannii* 15,9 %. La durée médiane du séjour à l'hôpital était de 29 jours, tandis que la durée moyenne était de 45 jours. Le taux de mortalité lié à la RAM était de 8,6 % (12). Les enfants âgés de moins de 6 ans représentaient 58,3 % des décès. Parmi les personnes décédées, les filles représentaient 66,7 % et celles dont le tuteur était au chômage 66,7 %.

### Conclusion

Plus d'un tiers des enfants atteints d'infections ESKAPE présentaient une RAM (35,3 %). Avec un taux de mortalité atteignant 8,6 %, ces statistiques se traduisent par un fardeau important en termes de mortalité et de prévalence dans le contexte de la population dans son ensemble.

**Mots Clés:** ESKAPE, AMR, Prévalence, Taux de létalité, Antibiotiques

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## Introduction

Antimicrobial resistance (AMR), defined by the World Health Organization (WHO) as the ability of bacteria, viruses, fungi, and parasites to withstand medicines designed to eliminate them, has become a major global health challenge [1]. Although AMR spans all microorganisms, resistance among bacteria is particularly alarming due to widespread misuse and overuse of antibacterial agents [2]. The problem is especially pronounced in low- and middle-income countries, where overcrowding, inadequate sanitation, self-medication, limited diagnostic capacity, and suboptimal healthcare practices contribute to the emergence and spread of multidrug-resistant (MDR) organisms.

The WHO has identified a critical group of MDR bacteria—*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp., collectively referred to as ESKAPE pathogens—as priority organisms requiring urgent surveillance and

drug development efforts [3]. These pathogens are major drivers of healthcare-associated infections and are associated with high morbidity, mortality, diagnostic challenges, and increased healthcare costs [4]. Children, particularly those from low-income settings, are disproportionately affected due to their developing immune systems and greater exposure to infectious environments [5].

Effective AMR surveillance is essential but remains limited in many resource-constrained settings. In Kenya, there is a notable scarcity of data on ESKAPE pathogens, especially in paediatric populations. No prior studies have examined the prevalence or mortality burden of AMR among ESKAPE infections at Kenyatta National Hospital (KNH), the national referral center. This study therefore aimed to determine the prevalence and case fatality rate of AMR in ESKAPE infections among children aged 12 years and below admitted to the paediatric wards of KNH between June 2019 and June 2022. The findings are intended to strengthen national AMR surveillance and

inform policy and clinical strategies to mitigate the growing threat of drug-resistant infections.

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## Material and Methods

The study was conducted at KNH, the largest tertiary health facility in East Africa and a teaching hospital. It is a 2000-bed hospital attending to approximately 60,000 inpatients and 450,000 outpatients every year. The study focused on children aged 1 month to 12 years admitted in the paediatric department, consisting of 4 wards and a clinic, and the microbiology laboratory at KNH, from June 2019 to June 2022 with ESKAPE infections. Laboratory records that either lacked corresponding patient files or missed important variables for the study were excluded. A retrospective cross-sectional study design was used. Fisher's formula was used to arrive at a sample size of 140, using a population estimate of 10% to determine the case fatality rate. The participants were determined using simple random sampling via a digital randomization application that generated random numbers from the total study population with allocated identification numbers.

Data was abstracted from microbiology laboratory records by the primary investigators. Only data records of patients stated in the approved proposal were accessed. Isolates from different biological specimens of the same patient – apropos of blood culture, urine culture, wound swabs, respiratory samples, and cerebrospinal fluid (CSF) samples – were considered as separate individual cases if they reflected different antibiotic susceptibility patterns at any given time, were isolated at least 7 days apart, and/or constituted different bacterial species within the ESKAPE group. After the selection of appropriate laboratory records to inform the study sample size, unique patient identifiers were noted for cross-referencing for identification of corresponding patient files in the wards and flagging duplicated data. The patient files were thereafter scrutinized using an abstraction tool to obtain the clinical and socio-demographic variables.

All information regarding specimens, patient records and laboratory results stored in the KNH electronic database were only accessible following ERC and KNH approval. Each study proforma was assigned a unique serial code to prevent data duplication and maintain patient confidentiality. The data was coded and entered into Microsoft Excel 2019 and secured by passwords only accessible by the investigators. All copies are stored in a file in an external hard drive that's password-protected and in sole custody of the principal investigator.

Statistical software, SPSS version 26 (Chicago, Illinois), was used to analyse the data, which was then summarized using descriptive statistics. The study population was described using clinical and socio-demographic characteristics, and each pathogen and group of pathogens, that is, gram-negative and gram-positive groups, were further sub-analysed. Patients having more than one organism were considered separate entities, and the highest resistance level was used. For the evaluation of patient mortality in relation to AMR, we conducted a linear and logistic regression analysis, factoring in the socio-demographics and source of the specimen. Group differences, case fatality rate, and associations were assessed and a P-value of less than 0.05 was interpreted as statistically significant. Continuous variables were presented using measures of central tendency and nominal variables by frequencies and percentages. The results will be presented using tables, where appropriate. Bacterial susceptibility patterns will be tabulated and presented as percentages.

Consent was obtained from the KNH/UON ERC and from KNH management. The hospital management gave a go-ahead which included a permit to retrieve patient files from the health records management department. The documents and data collected were held with confidentiality and the outcome of the analysis cannot allow re-identifying participants. The research posed minimal or no harm to the subjects under study (principle of non-maleficence).

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## Results

A total of 12,000 records were reviewed from the KNH microbiology laboratory and of these, 1155 records were eligible as the study population. 644 were boys (55.8%) and 511 were girls (44.2%). 140 individuals were sampled from this to determine the case fatality rate. This entailed a demographic of 86 boys (61.4%) and 54 girls (38.6%). 96 (68.6%) were below 6 years old, while 44 (31.4%) were between 6 and 12 years old. The majority of caregivers for the children were unemployed, 81 (57.9%) out of the total sample of 140.

The distribution of the 1155 ESKAPE isolates by clinical specimens reflected the following patterns of frequency: wound swabs 363 (31.4%), urine specimens 354 (30.6%), blood cultures 248 (21.5%), respiratory samples 176 (15.2%), and CSF 14 (1.2%). Of the 1155 isolated cases of ESKAPE infections, 408 had antimicrobial resistance, equating to a prevalence of 35.3%. The specific prevalence per pathogen is depicted in the table below.

**Table 1: Prevalence of AMR in ESKAPE Infections by Pathogens**

Bacterial Species	Without AMR	With AMR	Total	Prevalence (%) (With AMR/ Total x 100%)
Enterococcus spp.	138	45	183	24.6%
Staphylococcus aureus	156	78	234	33.3%
Klebsiella spp.	150	77	227	34.1%
Acinetobacter baumannii	51	65	116	56.0%
Pseudomonas aeruginosa	52	34	86	39.5%
Enterobacter spp.	200	109	309	35.3%
TOTAL	747	408	1155	35.3%

Additionally, AMR was found more in children under 6 years (68.6%), boys (61.4%), caregiver unemployment (57.9%), treatment with combination

therapy (70.7%), and invasive procedures (73.6%). However, most of the AMR cases did not have concomitant immunocompromised states.

**Table2: Descriptive Information on Sociodemographic and Clinical Characteristics**

	Definition	UDR	MDR	XDR	PDR	Total
Age Group	Under 6 years	23 (57.5%)	63 (75.0%)	6 (66.7%)	4 (57.1%)	96 (68.6%)
Sex	Boys	29 (72.5%)	47 (56.0%)	7 (77.8%)	3 (42.9%)	86 (61.4)
Caregiver Occupation	Unemployed	21 (52.5%)	48 (57.1%)	7 (77.8%)	5 (71.4%)	81 (57.9)
Immunocompromised Status	Yes	9 (22.5%)	23 (27.4%)	3 (33.3%)	1 (14.3%)	36 (25.7)
Treatment Regimen	Combination	25 (62.5%)	61 (72.6%)	7 (77.8%)	6 (85.7%)	99 (70.7)
Invasive Procedures	Yes	33 (82.5%)	58 (69.0%)	6 (66.7%)	6 (85.7%)	103 (73.6)
Duration of Hospital Stay (Days)	Median(IQR)	22(10-47)	36(19-61)	35(14-74)	21(13-31)	29 (15-56)
	Mean	36.9	51.2	49.7	22	45.9

The mortality rate in AMR was 8.6% (12). Of this, Enterobacter spp. accounted for the majority of the case fatalities at 41.7%, followed by Klebsiella spp. at 25%, Acinetobacter baumannii (16.7%), Staphylococcus aureus (8.3%), and Enterococcus faecium (8.3%). Pseudomonas aureguinosa had no reported case fatalities. However, the lethality of contraction of AMR

across each infection was highest with A. baumannii (22.2%), followed by Enterobacter spp. (11.3%), Klebsiella pneumoniae (11.1%), Enterococcus faecium (5%), and Staphylococcus aureus (3.6%). Those aged below 6 years accounted for 58.3% of the deaths. Of those who died, girls accounted for 66.7%, and those with caregiver unemployment 66.7%.

**Table 3: Mortality Distribution in ESKAPE AMR Categories by Sociodemographic Factors**

	Definition	UDR	MDR	XDR	PDR	Total
Age Group	Under 6 years	0 (0%)	4 (57.1%)	1 (50.0%)	2 (66.7%)	7 (58.3%)
Sex	Girls	0 (0%)	5 (71.4%)	1 (50.0%)	2 (66.7%)	8 (66.7%)
Caregiver Occupation	Unemployed	0 (0%)	4 (57.2%)	2 (100.0%)	2 (66.7%)	8 (66.7%)

## Discussion

The findings from this study on AMR among 1155 pediatric patients offer valuable insights that align with the broader global context highlighted in the introduction. There's critical concern of MDR organisms in low and middle-income countries (LMICs), particularly due to challenges such as poorly maintained healthcare facilities and inadequate resources [6]. This study's demographic distribution echoes these challenges, revealing vulnerabilities in healthcare systems grappling with resource limitations.

The prevalence data in this study, especially the higher proportion of boys (55.8%) and the majority below 6 years old (68.6%), resonates with the literature's depiction of global trends. Similar age and gender-related trends have been highlighted in multiple systematic reviews on AMR in Africa [7,8]. The disproportionate prevalence among younger children underscores the vulnerability of this demographic to AMR, aligning with the global burden outlined in the literature.

The distribution of ESKAPE isolates and their resistance patterns identified in the study correlates with the literature's assertion of a global challenge posed by AMR. A separate study done in Kenya, with findings emphasizing high resistance rates in A.

## Conclusion

The study's findings necessitate further alarm on the existing concerns imposed by the global repository on AMR prevalence and its associated mortality, specifically as related to ESKAPE pathogens. The prevalence of AMR among this group was found to be as high as 35.3%, indicating a significant burden of AMR in LMICs. ESKAPE AMR was also seen to be more predominant in boys than girls, in children below 6 years, and in those with caregiver unemployment. Further studies to detail the factors associated with the increment in prevalence across these socio-demographic groups will be crucial in efforts to curtail

baumannii, P. aeruginosa, E. coli, and K. pneumoniae, aligns with this study's identification of individual pathogens contributing differentially to the overall AMR prevalence [9].

Factors associated with higher AMR rates identified in the study, such as age below 6 years, caregiver unemployment, treatment with combination therapy, and invasive procedures, align with WHO's contention that antimicrobial resistance is driven by factors like the spread of resistant microorganisms, volume of antimicrobials used, and controllable factors [1].

The mortality rates and the pathogens contributing to fatalities in the study corroborate the global burden outlined in the literature. The demographic breakdown of deaths, particularly the prevalence among girls and those with caregiver unemployment, underscores the intersectionality of factors contributing to AMR-associated mortality, agreeing with the assertion that overarching factors are invariably influenced by socioeconomic factors [10].

## Study Limitation

Failure to establish temporal relationships of factors, since only a retrospective cross-sectional study was conducted.

Only limited to paediatric groups

the AMR epidemic.

Moreover, the mortality rate among children with ESKAPE-associated AMR was 8.6%, implying that about 1 person in every 10 that have this diagnosis succumb. This is a remarkably high proportion, and aggressive and precise treatment protocols need to be put in place to manage the condition.

## Recommendations

In order to enhance our understanding and guide the initiation of empirical therapy, it is imperative to conduct further studies on susceptibility patterns associated with ESKAPE infections. Additionally, a prudent approach to healthcare involves vigilant monitoring of children below the age of 6 during

admissions for infectious diseases. The judicious use of empirical antimicrobial therapy, coupled with timely transitions from combination to targeted therapy, is recommended for effective patient care. Adherence to infection prevention protocols, including the minimization of invasive techniques and optimization of aseptic practices, is essential to maintain healthcare standards. To mitigate the spread of resistant strains, it is crucial to identify and isolate cases with resistance, coupled with efforts to reduce the duration of hospital stays. Collectively, these measures contribute to a comprehensive strategy aimed at improving the management and prevention of infectious diseases in healthcare settings.

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## Conflict of Interest

Authors do not declare any conflict of interest

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