Ethiopian Food and Drug Authority (EFDA)

Trends in Antimicrobial Consumption in Ethiopia: A Surveillance Report 2020-2022

Addis Ababa, Ethiopia

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Abstract

Background: Antimicrobial resistance (AMR) poses a severe global health threat, driven by the overuse and misuse of antimicrobials across the human, agricultural, and veterinary sectors. To combat this, global and national AMR prevention and containment strategies have been implemented, necessitating continuous monitoring of antimicrobial consumption (AMC) as an integral part of antimicrobial stewardship interventions.

Objective: This study aims to assess and analyze trends in AMC in Ethiopia from 2020 to 2022, with the goal of informing national and sub-national strategies to combat AMR.

Methods: A three-year AMC surveillance was conducted from 2020 to 2022. Data on locally manufactured and imported antimicrobials were collected from local manufacturers and Ethiopian Food and Drug Authority (EFDA)-regulated ports of entry, respectively. AMC was analyzed using the WHO GLASS AMC tool, with antimicrobials categorized using the WHO Anatomical Therapeutic Chemical (ATC) classification system. Consumption was measured in Defined Daily Doses (DDDs) and DDD per 1,000 inhabitants per day (DID), normalized using population estimates from the World Population Prospects.

Results: The total AMC in Ethiopia increased from 432 million DDDs in 2020 to 485 million DDDs in 2022. The DID rose from 10.63 in 2020 to 11.34 in 2022. Antibacterials dominated consumption, comprising 98.87% in 2020, 95.96% in 2021, and 99.79% in 2022. Penicillins (J01C) and quinolones (J01M) were the most consumed antimicrobials. The majority of antibacterial agents consumed were in the Access group, accounting for 71.14% in 2020, 70.65% in 2021, and 74.2% in 2022. Oral formulations consistently made up over 87% of the total consumption each year. Reliance on imported antimicrobials remained high, with imports comprising 64.76% in 2020 and 74.47% in 2022.

Conclusion: The increasing trend in AMC in Ethiopia from 2020 to 2022 underscores the urgent need to establish and strengthen national, sub-national, and facility-level surveillance and reporting systems to better monitor and manage antimicrobial use.

Key words: Antimicrobial consumption, antimicrobial resistance, Ethiopia, Defined Daily Doses, DDD, WHO ATC classification, AWaRe.

Table of Contents

List of Tables

List of Figures

Abbreviation and Acronyms

AMC:	Antimicrobial Consumption
AMR:	Antimicrobial Resistance
ATC:	Anatomical Therapeutic Classification
AWaRe:	Access, Watch, and Reserve
COVID-19:	Coronavirus Disease 2019
DDD:	Defined Daily Dose
DID:	DDD per 1,000 inhabitants per day
EFDA:	Ethiopian Food and Drug Authority
GLASS:	Global Antimicrobial Resistance and Use Surveillance System
RoAs:	Route of Administrations
WHO:	World Health Organization

Acknowledgements

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Our sincere appreciation goes to the World Health Organization (WHO) for their invaluable support and guidance throughout the surveillance process. Their contributions were instrumental in ensuring the completion of this report. We also recognize the exceptional technical team for their expertise and tireless efforts in preparing and analyzing the data for this report.

Finally, we extend our thanks to all individuals and stakeholders who provided valuable feedback and insights during the review process, ensuring the quality and relevance of this surveillance report.

Introduction

Antimicrobial resistance (AMR) is a critical global health issue of the 21st century [1], driven by the overuse and misuse of antimicrobials in human and animal health, and as well as in agriculture. This widespread misuse accelerates the development of resistant microorganisms [2], leading to ineffective treatment, prolonged illness, increased mortality, and higher healthcare costs [3-5]. Ethiopia, like many other low- and middle-income countries, faces significant challenges in combating AMR due to limited healthcare infrastructure, inadequate surveillance systems, and insufficient public awareness [6-12].

Monitoring antimicrobial consumption (AMC) is essential for generating evidence for combating AMR effectively [13-16]. AMC data provide critical insights into prescribing practices, trends in drug consumption, and areas requiring targeted interventions [17-19]. Such data are vital for formulating policies and programs aimed at promoting the rational use of antimicrobials and mitigating resistance. However, comprehensive data on national AMC trends over extended periods have been scarce in Ethiopia, creating a significant knowledge gap [20]. Previous studies have highlighted issues such as self-medication, over-the-counter availability of antimicrobials, and non-adherence to treatment guidelines [21], but these studies were often limited in scope and duration, failing to provide a complete picture of AMC across the country [22, 23]. This knowledge gap hinders the development of effective AMR containment strategies, underscoring the urgent need for a thorough analysis of antimicrobial use trends [24-28].

This study aims to address this gap by assessing and analyzing AMC trends in Ethiopia from 2020 to 2022. The findings will offer a detailed overview of AMC patterns at the national level, providing essential insights for policymakers, healthcare providers, and other stakeholders to make evidence-based decisions aimed at curbing AMR in Ethiopia.

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Rationale

AMR poses a significant threat to global health, economic stability, and societal well-being. The resistance of bacteria, viruses, fungi, and parasites to standard treatments results in harder-to-treat infections, longer hospital stays, higher medical costs, and increased mortality [4, 29-34]. In Ethiopia, the rise of AMR is particularly challenging for the already strained healthcare system [35, 36] necessitating a multifaceted approach that begins with a thorough understanding of AMC patterns [1, 12, 37].

Monitoring AMC is critical for combating AMR, as it provides evidence to guide policy and practice. Surveillance of AMC serves as a proxy indicator to identify misuse and overuse, which are the primary drivers of resistance [15, 16, 38-40]. Despite its importance, Ethiopia lacks comprehensive, long-term data on AMC which hampers the development of targeted interventions and policies for rational antimicrobial use [41-43]. Addressing this data gap is crucial for implementing effective AMR containment strategies tailored to Ethiopia's specific context [44-47].

Objectives

General Objective

- To assess and analyze the trends in AMC in Ethiopia from 2020 to 2022.

Specific Objectives

- To quantify the overall AMC in Ethiopia during the three-year period (2020-2022)
- To examine the consumption patterns of different classes of antimicrobials
- To develop evidence-based recommendations for improving antimicrobial stewardship policies and practices in Ethiopia.

Methods

Study Area and Design

The study encompassed the entire country of Ethiopia, with specific data collection points at ports of entry, including Cargo Terminal and Kality in Addis Ababa, Modjo, Moyale, Semera, and Dire Dawa. Data were also collected from local manufacturers to ensure comprehensive coverage across the country. This study employed a retrospective observational design to analyze AMC in Ethiopia over a three-year period from 2020 to 2022.

Data Source and Validation

Data were sourced from the Ethiopian Food and Drug Authority's (EFDA) eRIS import records and local manufacturing data, providing comprehensive information on the production and importation of antimicrobial products. The collected data were rigorously validated by cross-referencing with importers' records and local manufacturing data where possible to ensure accuracy and reliability. This validation process was crucial for obtaining a precise understanding of the total volume of antimicrobials available in the country.

Eligibility Criteria

Antimicrobials, including antibacterials, antivirals, antimycotics, and antifungals, were included in the surveillance if they were classified under the WHO Anatomical Therapeutic Chemical (ATC) Classification system and had an associated Defined Daily Dose (DDD). Antimicrobials not classified under the WHO ATC system, those lacking DDDs, or those with incomplete data were excluded from the analysis.

Classification and Measurement

Antimicrobials are classified according to the ATC classification system, and the volume of consumed antimicrobials is expressed as DDDs. Only products associated with ATC/DDD listed in the ATC/DDD 2023 index are included in the analysis. The classifications include five main antimicrobial classes:

- Antibacterials (ATC J01, A07AA, P01AB)
- Antimycotics and antifungals for systemic use (ATC J02, D01B)
- Antivirals for systemic use (ATC J05)
- Drugs for the treatment of tuberculosis (ATC J04A)

- Antimalarials (ATC P01B)

Data Collection Timeline

Data on AMC were collected annually from 2020 to 2022. For each year, data collection was conducted from January to December, ensuring a comprehensive annual dataset. The data were compiled and analyzed early in the following year to allow for a timely assessment of trends and patterns. This timeline was chosen to capture seasonal variations and other temporal factors that could influence consumption patterns.

Data Collection Instruments and Procedures

AMC data were systematically collected using data abstraction sheets from eRIS and manufacturing records. To ensure completeness, additional data were requested from stakeholders via email. The WHO GLASS AMC data entry format was utilized for data entry and analysis to maintain alignment with global standards.

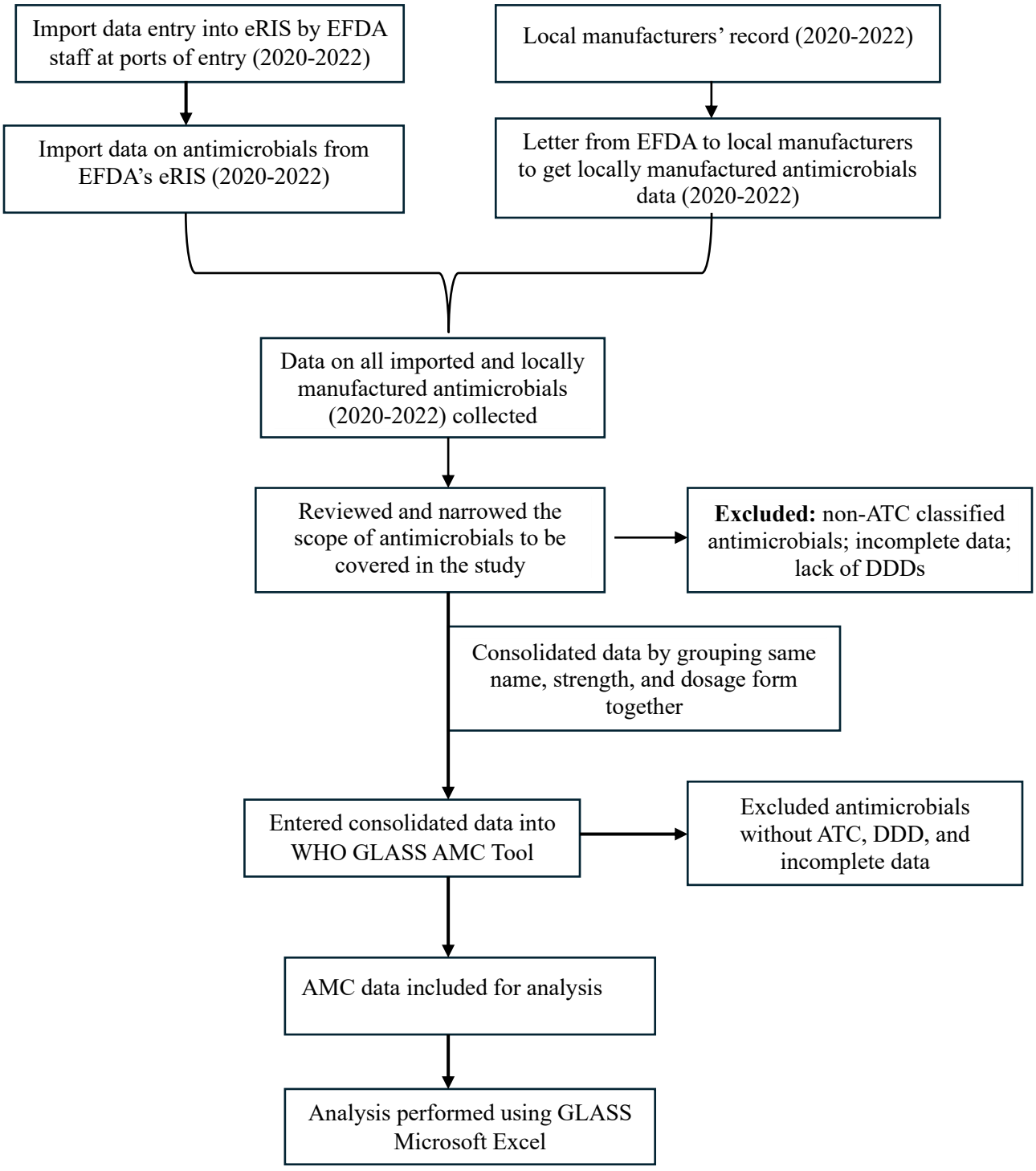

Figure 1: Data collection and cleaning methodology for the Ethiopia national antimicrobial consumption analysis

Data Quality Management

To ensure data quality, several measures were implemented. Training sessions were provided for data collectors on the use of data collection tools, procedures, and data abstraction sheets. The WHO GLASS AMC Macro Automated Validation Tool was employed to ensure data completeness, consistency, accuracy, and conformity. Additionally, data verification involved cross-checking import data with records from importers to ensure accuracy and consistency throughout the process.

Metrics and Data Analysis

The volume of antimicrobials consumed was presented using two metrics: DDD and the weight of antimicrobial substances in metric tonnes. Consumption was reported for total care, incorporating both imported and locally manufactured data. It was expressed as DDDs per 1,000 inhabitants per day, and relative consumption was also calculated. Population data were obtained from the World Population Prospects 2020-2022 and adjusted according to the system coverage level provided by the country when below 95%. To assess the relative consumption of antibacterials by AWaRe categories, both the WHO 2023 and Ethiopia 2020 AWaRe classifications were applied.

Data analysis was conducted using the WHO GLASS AMC Microsoft Excel-Based Tool. The collected data were cleaned, validated, and organized for analysis. Descriptive statistics were used to summarize the data, and trends in AMC were analyzed using DDDs, total volume in DDDs, metric tonnes, and DDDs per 1,000 inhabitants per day. Results were presented in both tabular and graphical formats to facilitate easy interpretation.

Table 1: Data contextual information as per GLASS database

Year	Population (WPP*)	Population Coverage	Population Used for Analysis	Level	Sources of Data	ATC Classes Reported
2022	123,379,924	95%	117,210,927	Import/Local Manufacturing	Production for domestic market, Import records	J01, J02, J05, P01AB, P01B
2021	120,283,026	95%	114,268,874	Import/Local Manufacturing	Production for domestic market, Import records	D01BA, J01, J02, J05, P01AB, P01B
2020	117,190,911	95%	111,331,365	Import/Local Manufacturing	Production for domestic market, Import records	D01BA, J01, J02, J05, P01AB, P01B

Ethical Considerations

A permission letter from the EFDA General Director was submitted to local manufacturers, EFDA's central branch office (responsible for controlling ports of entry), and the Medicines Registration and Licensing Directorate to obtain all necessary data. All data were handled with strict confidentiality, and measures were taken to ensure that individual data sources were anonymized and protected throughout the analysis process.

Results

Overall Antimicrobial Consumption in Tons and Defined Daily Dose

Despite majority of the consumed antimicrobials being from antibacterial (JO1, A07AA, P01AB) group, the total volume of antimicrobials consumed regardless of the group was 532.23 tons and 431,972,986.1 DDD in 2020; 692.975 tons and 547,659,483.1 DDD in 2021, and 608.72 tons and 485,320,971.8 DDD in 2022. The three-year average total AMC in Ethiopia was 488,317,813.7 DDD (Table 2).

Table 2: A three-year antimicrobial consumption expressed in tons and DDD in Ethiopia

Pharmacological subgroups	**2020**		**2021**		**2022**		**Three years DDD Average**
	Tons	DDD	Tons	DDD	Tons	DDD	
Antibacterial (JO1, A07AA, P01AB)	531.1	427,069,849.1	687.8	525,404,773.7	608.1	484,188,917.8	478,887,846.9
Antimycotics and antifungals for systemic use (JO2, D01B)	0.87	4,264,382.4	3.28	1,4036,306.0	0.10	500,000.0	6,266,896.13
Antimalarials (P01B)	0.14	608,857.1	1.59	5,676,618.4	0.05	169,607.1	2,151,694.2
Antivirals for systemic use (JO5)	0.12	29,897.5	0.31	2,541,785.0	0.47	462,446.9	1,011,376.47
Total	**532.23**	**431,972,986.1**	**692.98**	**547,659,483.1**	**608.72**	**485,320,971.8**	**488,317,814**

Overall antimicrobial consumption in DDD per 1000 inhabitants per day (DID)

The AMC in Ethiopia in DID from 2020 to 2022 was found to be 10.63, 13.131 and 11.344, respectively. Almost all antimicrobials consumed in Ethiopia for the three years period were from the antibacterial group (JO1, A07AA, P01AB) that accounted for 98.87%, 95.96% and 99.79%, followed by antimycotics and antifungals for systemic use (JO2, D01B) that accounted 0.94%, 2.59% and 0.09%, respectively. The orally administered antimicrobial consumption was accounted 87.96%, 87.5% and 91.24% in 2020, 2021 and 2022, respectively. The highest parental AMC was reported in the year 2021 (12.5%). The total DID and respective antimicrobial group DID for each year are summarized in Table 3.

Table 3: A three years antimicrobial consumption in Ethiopia as per DDD per 1000 inhabitants per day (DID)

Category		**2020**		**2021**		**2022**		**A three year average**	
		DID	%	DID	%	DID	%	DID	%
Antimicrobial group	Antibacterials*	10.51	98.87	12.60	95.96	11.32	99.79	11.48	98.10
	Antimycotics and antifungals for systemic use	0.10	0.94	0.34	2.59	0.010	0.09	0.15	1.30
	Antimalarials	0.015	0.14	0.136	1.04	0.004	0.04	0.024	0.44
	Antiviral for systemic use	0.001	0.01	0.061	0.46	0.011	0.10	0.0467	0.21
	Total	**10.63**		**13.13**		**11.34**		**11.70**	
Route of ...	Oral	9.35	87.96	11.49	87.5	10.35	91.24	10.397	88.88
	Parenteral	1.28	12.04	1.64	12.5	1.00	8.76	1.301	11.12
	Total	**10.63**		**13.13**		**11.34**		**11.70**	

*Agents against amoebiasis and other protozoal diseases such as metronidazole and tinidazole are included as antibacterials

Antimicrobial Consumption by Source

In 2020, all antivirals for systemic use and antimycotics and antifungals for systemic use were from import. Whereas in 2021, 1.64% of antivirals for systemic use and 51.93% of antimycotics and antifungals for systemic use were locally manufactured. In 2022, locally manufactured antivirals for systemic use were increased to 10% and none of antimycotics and antifungals for systemic use were locally manufactured. However, all antimalarials were from import throughout the reporting period 2020-2022 (Table 4).

Table 4: Antimicrobial consumption in Ethiopia as per the source of antimicrobials and DDD/1000 inhabitants/day (DID) per antimicrobial source

Antimicrobial group	**2020, DID (%)**			**2021, DID (%)**			**2022, DID (%)**		
	Local*	Imported	**Total**	Local*	Imported	**Total**	Local*	Imported	**Total**
Antibacterials*	3.746(35.65)	6.763(64.35)	**10.509**	3.090(24.53)	9.508(75.47)	**12.598**	2.895(25.58)	8.423(74.42)	**11.318**
Antiviral for systemic use	0.00(0.00)	0.001(100.0)	**0.001**	0.001(1.64)	0.060(98.34)	**0.061**	0.001(10.00)	0.009(90.00)	**0.01**
Antimycotics and antifungals for systemic use	0.00(0.00)	0.105(100.0)	**0.105**	0.175(51.93)	0.162(48.07)	**0.337**	0.00(0.00)	0.012(100.00)	**0.012**
Antimalarials	0.00(0.00)	0.015(100.0)	**0.015**	0.00(0.00)	0.136(100.0)	**0.136**	0.00(0.00)	0.004(100.00)	**0.004**
Total	**3.746 (35.24)**	**6.884(64.76)**	**10.63**	**3.266(24.87)**	**9.866(75.13)**	**13.131**	**2.896(25.53)**	**8.448(74.47)**	**11.344**

***Locally manufactured

As described in Figure 1 below, most of the antimicrobials consumed in Ethiopia were from import. In 2020, 64.76% of antimicrobials consumed as per the DID were from import. Similarly, in 2021 and 2022, 75.13% and 74.47% antimicrobials consumed as per the DID were sourced from imports, respectively.

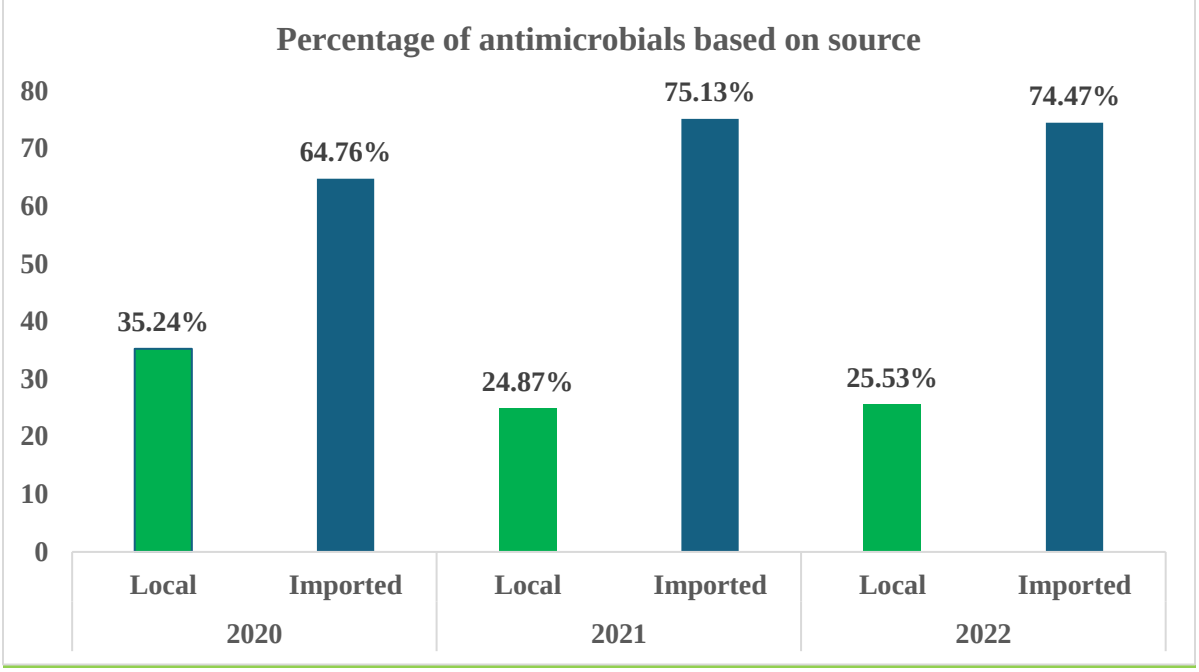

Figure 2: Antimicrobial consumption in Ethiopia based on the source

Antibacterial Consumption by Subgroups

Penicillin (39.65% in 2020, 35.88% in 2021, and 37.78% in 2022) and quinolone (25.59% in 2020, 20.56% in 2021, and 21.80% in 2022) antibacterial subgroups (ATC level 3 and level 4), followed by agents against amoebiasis and other protozoal diseases (15.0% in 2020, 13.5% in 2021, and 15.1% in 2022), were the most commonly consumed agents throughout the reporting period. The extended spectrum penicillin consumption trend increased from 66.9% in 2020 to 79.0% in 2022. The consumption trend of macrolides and lincosamides decreased from 6.22% in 2020 to 1.34% in 2022. The consumption of 1st and 2nd generation cephalosporin was decreased as opposed to increased consumption of 3rd generation cephalosporin's. In addition, the consumption of tetracycline's increased from 6.17% in 2020 to 13.02% in 2022 (Table 5).

Table 5: Antimicrobial consumption in Ethiopia based on antibacterial subgroup

Antibacterial subgroup		2020		2021		2022	
		DID	%	DID	%	DID	%
Penicillin **(J01C)**		4.17	39.65	4.52	35.88	4.28	37.78
ATC Level 4	Penicillin with extended spectrum (J01CA)	2.79	66.9	3.30	73.0	3.38	79.0
	Beta-lactamase sensitive penicillins (J01CE)	1.07	25.6	0.82	18.2	0.67	15.6
	Beta-lactamase resistant penicillins (J01CF)	0.31	7.5	0.40	8.8	0.23	5.4
	Combinations of penicillins, incl. beta-lactamase inhibitors (J01CR)	0.00	0.00	0.00	0.00	0.00	0.00
Other beta-lactam antibacterials **(J01D)**		0.41	3.92	1.55	12.28	0.68	6.05
ATC Level 4	1st generation cephalosporin's (J01DB)	0.20	49.3	0.56	36.4	0.17	25.5
	2nd generation cephalosporin's (J01DC)	0.02	5.6	0.01	0.86	0.002	0.07
	3rd generation cephalosporin's (J01DC)	0.18	44.8	0.97	62.5	0.51	74.4
	4th generation cephalosporin's (J01DC)	0.004	0.20	0.001	0.09	0.003	0.05
	Monobactams (J01DF)	0.00	0.00	0.00	0.00	0.00	0.00
	Other cephalosporins & penems (J01DI)	0.00	0.00	0.00	0.00	0.00	0.00
	Carbapenems (J01DH	0.03	0.13	0.04	0.19	0.002	0.04
Quinolone **(J01M)**		2.69	25.59	2.59	20.56	2.47	21.80
Anti-amoebiasis and other protozoal diseases **(P01AB)**		1.58	15.00	1.70	13.50	1.709	15.10
Macrolides, and lincosamides **(J01F)**		0.65	6.22	0.51	4.02	0.15	1.34
Tetracycline's **(J01A)**		0.65	6.17	1.01	7.99	1.47	13.02
Sulfonamides and trimethoprim **(J01E)**		0.29	2.77	0.62	4.96	0.49	4.34
Aminoglycoside **(J01G)**		0.05	0.44	0.07	0.56	0.05	0.46
Amphenicols **(J01B)**		0.02	0.17	0.03	0.24	0.01	0.09
Other antibacterials **(J01X)**		0.01	0.07	0.00	0.00	0.00	0.02

Antibacterial Consumption by AWaRe Classification

The Access category, which includes antimicrobials recommended as the first or second choice for most common infections, dominated the consumption in Ethiopia, accounting for 71.14% in 2020, 70.65% in 2021, and 74.20% in 2022. This is slightly higher compared to consumption reported as per WHO AWaRe classification, which was 66.20% in 2020, 67.60% in 2021, and 72.30% in 2022. The Watch category, which comprises antimicrobials with a higher potential for resistance, constituted 24.64% of the consumption in 2020, 24.69% in 2021, and 24.73% in 2022 in Ethiopia. The Reserve category, which includes last-resort antimicrobials, had minimal consumption in Ethiopia, with 0.03% in 2020, 0.06% in 2021, and 0.02% in 2022 (Table 6).

Table 6: Antimicrobial consumption in Ethiopia based on AWaRe classification

AWaRe classification		**2020**		**2021**		**2022**	
		DID	**%**	DID	**%**	DID	**%**
Ethiopia AWaRe category							
	Access	7.56	71.14	9.28	70.65	8.42	74.20
	Watch	2.62	24.64	3.24	24.69	2.81	24.73
	Reserve	0.003	0.03	0.01	0.06	0.003	0.02
	Not classified	0.45	4.19	0.60	4.60	0.12	1.05
	Total	**10.63**		**13.13**		**11.34**	
WHO AWaRe category							
	Access	6.95	66.20	8.51	67.60	8.19	72.30
	Watch	3.55	33.80	4.09	32.40	3.13	27.7
	Reserve	0.00	0.00	0.00	0.00	0.00	0.00
	Not classified	0.00	0.00	0.00	0.00	0.00	0.00
	Total	**10.51**		**12.60**		**11.32**	

DU75 and DU90 of antimicrobial consumption

The most consumed antimicrobials that made up 75% (DU75) of the overall consumption included amoxicillin, ciprofloxacin, metronidazole, procaine benzyl penicillin, and doxycycline from 2020-2022. These antimicrobials also prominently featured in the 90% consumption (DU90) category along with additional antimicrobials like azithromycin, cloxacillin, sulphamethoxazole + trimethoprim, and ceftriaxone.

The most commonly consumed oral formulations within the DU75 category were amoxicillin, ciprofloxacin and metronidazole, consistently across the years. Procaine benzyl penicillin was the most consumed parenteral antimicrobial, making up a substantial portion of the DU75 category each year. Ceftriaxone was the next most consumed parenteral antimicrobial, featuring prominently in the DU90 category, particularly in 2021 and 2022 (Table 7).

Table 7: DU75 and DU90 antimicrobial consumption in Ethiopia as per route of administration

		2020		2021		2022	
Antimicrobial substance		DU75	DU90	DU75	DU90	DU75	DU90
Overall	Amoxicillin (J01CA04)	24.73	24.73	22.15	22.15	27.00	27.00
	Ciprofloxacin (J01MA02)	22.74	22.74	17.22	17.22	20.24	20.24
	Metronidazole (J01XD01)	13.58	13.58	12.65	12.65	14.35	14.35
	Procaine benzyl penicillin (J01CE09)	10.01	10.01	6.19	6.19	--	5.87
	Doxycycline (J01AA02)	6.10	6.10	7.67	7.67	12.99	12.99
	Azithromycin (J01FA10)	--	3.22	--	3.08	--	--
	Cloxacillin (J01CF03)	--	2.93	--	3.03	--	2.05
	Sulphamethoxazole + trimethoprim (J01EE01)	--	2.74	4.76	4.76	--	4.33
	Ceftriaxone (J01DD04)	--	--	4.59	4.59	--	1.91
	Norfloxacin (J01MA06)	--	2.55	--	--	--	--
	Cephalexin (J01DB01)	--	1.89	--	4.28	--	--
	Ampicillin (J01CA01)	--	--	--	2.97	--	2.78
	Cefixime (J01DD08)	--	--	--	2.73	--	2.49
	Number of antimicrobials	**5**	**10**	**7**	**12**	**4**	**10**
Oral	Amoxicillin (J01CA04)	28.13	28.13	25.32	25.32	29.60	29.60
	Ciprofloxacin (J01MA02)	25.60	25.60	18.93	18.93	22.19	22.19
	Metronidazole (J01XD01)	15.39	15.39	14.23	14.23	15.66	15.66
	Doxycycline (J01AA02)	6.94	6.94	8.76	8.76	--	14.24
	Azithromycin (J01FA10)	--	3.66	--	**3.52**	--	--
	Cloxacillin (J01CF03)	--	3.34	--	**3.46**	--	--
	Sulphamethoxazole + trimethoprim (J01EE01	--	3.11	5.43	5.43	--	4.75
	Norfloxacin (J01MA06)	--	2.90	--	--	--	--
	Cephalexin (J01DB01)	--	2.10	4.89	4.89	--	--
	Ampicillin (J01CA01)	--	--	--	3.24	--	--
	Cefixime (J01DD08)	--	--	--	3.11	--	--
	Number of antimicrobials	4	9	**6**	**10**	**3**	**5**
Parenteral	Procaine benzyl penicillin (J01CE09)	82.81	82.81	49.59	49.59	66.81	66.81
	Ceftriaxone (J01DD04)	--	10.30	36.76	36.76	21.71	21.71
	Gentamycin (J01GB03)	--	--	--	--	--	5.26
	Ciprofloxacin (J01MA02)	--	--	--	5.21	--	--
	Number of antimicrobials	**1**	**2**	**2**	**3**	**2**	**3**

Antimalarial consumption based on substance

As depicted in Figure 2, the antimalarial consumption was higher in 2021 compared to other years, with artemether plus lumefantrine accounting for the highest proportion (0.127 DID out of 0.136 DID). However, in 2021, artemether consumption was zero, as opposed to its consumption in 2020 (0.004 DID out of 0.015 DID). In addition, the consumption of artesunate in 2021 was 0.009 DID, but it was zero in 2020 and 2022.

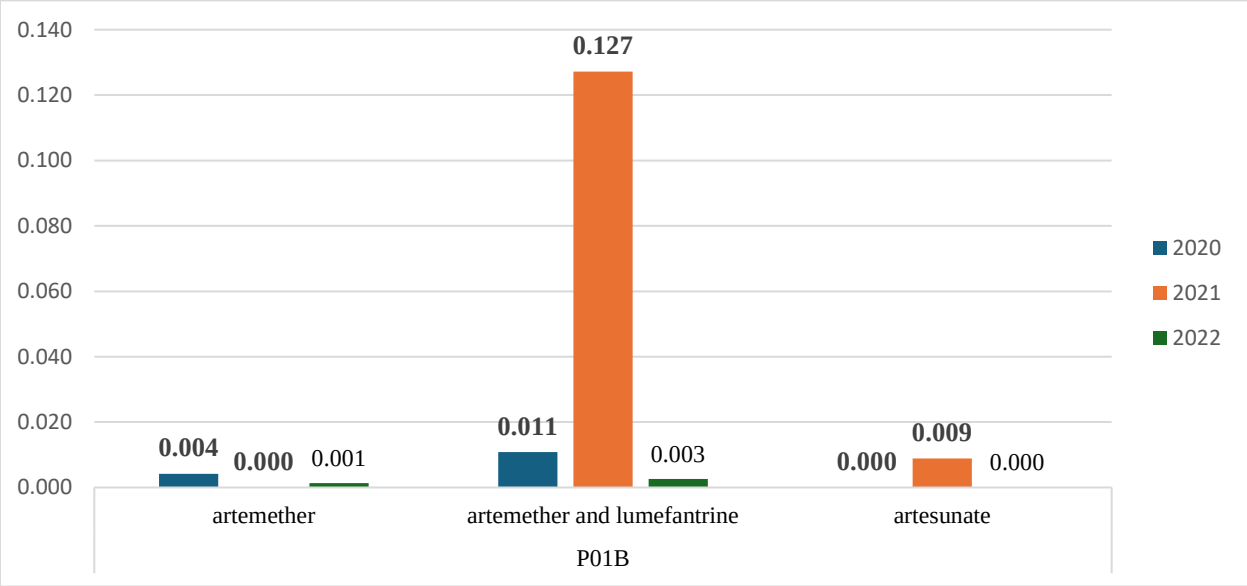

Figure 3: Antimalarial consumption by substance per DDD per 1000 inhabitants per day (DID)

Discussion

The analysis of AMC in Ethiopia from 2020 to 2022 reveals significant trends and insights crucial for addressing the challenges posed by AMR in the country. The findings highlight patterns in overall consumption, sources of antimicrobials, and the distribution across different antibacterial subgroups, routes of administration, and AWaRe classification.

The analysis of AMC in Ethiopia from 2020 to 2022, measured in DID, revealed a notable increase from the previous three years (2017-2019), with values rising from 8.50 in 2017 to 10.00 in 2019 and further to an average of 11.70 in the 2020-2022 period, peaking at 13.13 in 2021[20]. This trend contrasts sharply with the higher DID values observed in Uganda and Tanzania during the same periods. Uganda, for instance, experienced a peak DID of 123.30 in 2019, followed by a significant decline to 29.02 in 2021, reflecting a possible impact of the COVID-19 pandemic on healthcare practices and antimicrobial use [48]. Similarly, Tanzania maintained high DID values before the pandemic, with 93.11 in 2017 and 80.80 in 2019, indicating a consistently high level of AMC [49]. In contrast, high-income countries like the United Kingdom and the United States either maintained stable or declining DID values during the pandemic, reflecting the effectiveness of established antimicrobial stewardship programs in these regions [50]. The comparison underscores the variability in AMC across different regions, with Ethiopia showing a more controlled but increasing trend, while Uganda and Tanzania exhibited higher but more fluctuating patterns, and high-income countries maintained more stable consumption levels.

The data indicate a strong reliance on imported antimicrobials, with over 64% of antimicrobials being imported each year. This dependency on imports underscores the challenges faced by the local pharmaceutical manufacturing sector in meeting the national demand for antimicrobials. The consistently high percentage of imported antimicrobials, peaking at 75.13% in 2021, reflects the need for policies to strengthen local production capabilities. Similarly, other studies in African countries such as Nigeria and Kenya have shown that local production capabilities are limited [51]. This reliance poses significant risks during global supply chain disruptions, as seen during the COVID-19 pandemic, highlighting vulnerabilities in accessing essential medicines. The pandemic-induced disruptions in global supply chains have underscored the urgent need for Ethiopia to strengthen its local pharmaceutical manufacturing sector. Enhancing local production capabilities would not only

improve the resilience of the healthcare system but also reduce dependency on international supply chains [52, 53].

Penicillins and quinolones were the most commonly consumed antibacterial subgroups throughout the reporting period, accounting for significant proportions of the total AMC. Penicillins comprised 39.65% in 2020, 35.88% in 2021, and 37.78% in 2022, while quinolones made up 25.59%, 20.56%, and 21.80%, respectively. The high consumption of these subgroups reflects their broader use and availability in treating prevalent infections, which aligns with previous consumption reports [20] and Ethiopian standard treatment guidelines. In addition, Another study on antimicrobial use in low- and middle-income countries similarly found high usage of penicillins and quinolones [54]. However, the decline in the consumption of macrolides and lincosamides from 6.22% in 2020 to 1.34% in 2022 indicates shifting prescribing practices, likely influenced by initial explorations of azithromycin as a potential treatment for COVID-19. The reduced use could be attributed to a decline in COVID-19 cases and a corrective trend as more evidence emerged regarding the low efficacy of azithromycin in treating COVID-19 [55-57].

Oral formulations were predominant, consistently accounting for over 87% each year. The proportion of orally administered antimicrobials increased from 87.96% in 2020 to 91.24% in 2022. This trend toward high consumption of oral formulations might be driven by their convenience, ease of use, and patient compliance. However, to achieve the most efficient and cost-effective management of infections in outpatient settings, accessible and effective oral antimicrobial options are crucial. The data highlight the important role of antimicrobial stewardship and patient education in ensuring the appropriate and responsible use of these essential medications, particularly in community settings where regulation and monitoring may be less stringent [58].

The majority of antimicrobials consumed in Ethiopia fell under the Access category of AWaRe classification (>70% and >66% as per Ethiopian and WHO AWaRe classification, respectively), exceeding the WHO target of >60% consumption in the Access group. The Watch category, which includes antimicrobials with higher resistance potential, constituted around 24-25% of the total consumption. The minimal use of Reserve category antimicrobials, ranging from 0.02% to 0.06%, is encouraging as it indicates limited reliance on last-resort drugs, addressing concerns about AMR. However, the presence of a small proportion of antimicrobials not classified under the Ethiopian AWaRe classification suggests

the need for further revision of the AWaRe classification to include all antimicrobials available in the country. Currently, the Ethiopian AWaRe classification only includes antimicrobials listed in the 2020 Essential Medicines List [59]. This need for revision is supported by similar observations in other countries such as Tanzania and Uganda. A higher and almost similar proportion of Access group AMC was reported in the Tanzanian (>90%) [49] and Ugandan study (>65 %) [48], respectively.

Amoxicillin, ciprofloxacin, metronidazole, procaine benzyl penicillin, and doxycycline accounted for 75% (DU75) of the overall consumption of antimicrobials in Ethiopia. Additional antimicrobials such as azithromycin, cloxacillin, sulphamethoxazole + trimethoprim, and ceftriaxone contributed to 90% (DU90) of overall antimicrobial consumption. The dominant consumption of oral amoxicillin, ciprofloxacin, and metronidazole, and parenteral procaine benzyl penicillin followed by ceftriaxone, underscores the importance of focusing stewardship efforts to ensure their continued effectiveness in Ethiopia. In contrast, the Tanzanian national AMC survey showed a slightly different pattern, with doxycycline followed by amoxicillin, sulphamethoxazole + trimethoprim, erythromycin, and metronidazole making up their DU75, and procaine benzyl penicillin being the leading parenterally administered antimicrobial [49]. Additionally, the previous AMC survey from 2017-2019 in Ethiopia indicated higher consumption of Doxycycline followed by Norfloxacin, Azithromycin and Ciprofloxacin [20]. The higher overall three-year consumption of doxycycline in the previous report might be attributed to an acute watery diarrhea outbreak in 2017.

The use of import data and local manufacturing data, sourced from both paper-based and electronic database records using the WHO GLASS AMC survey standardized methodology and robust analysis techniques, to estimate national-level consumption was a strength of this study. This approach permits comparisons over time and across countries. However, these strengths must be balanced with a critical understanding of the study's limitations to ensure that the conclusions drawn are both accurate and actionable. Key limitations include:

- Antimicrobials without ATC codes and DDD values as per WHO methodology were not included in the survey.
- Imported and locally manufactured data at the national level were used as proxy indicators for use, which may not reflect the actual use of antimicrobials.

- Only antimicrobials imported through recognized routes were included in the study, but there may be antimicrobials entering the country through illegal and unregulated routes, which could affect the real consumption data.
- The study only included antimicrobials intended for human consumption and does not reflect overall antimicrobial consumption across human and animal health sectors.

While the study's strengths highlight its valuable contributions, acknowledging its limitations is crucial for interpreting the results and drawing meaningful conclusions. These limitations provide important insights for future research efforts, particularly emphasizing the need for robust data collection, diverse data sources, and a nuanced understanding of the local context.

Conclusion

The findings from this study have significant implications for AMR prevention and containment strategies in Ethiopia. The high reliance on imported antimicrobials underscores the urgent need for strategies to boost local production, thereby ensuring a stable and sustainable supply of essential medicines. This is critical for supporting the fourth strategic objective of Ethiopia's National Action Plan on AMR, which focuses on the prudent use of antimicrobials. Targeted interventions should be developed to address the consumption patterns observed in different antibacterial subgroups and routes of administration, promoting rational use and reducing the risk of resistance. The dominance of Access category antimicrobials suggests that stewardship efforts should prioritize ensuring their appropriate use while closely monitoring and controlling the use of Watch and Reserve categories to mitigate the development of resistance. These findings should inform policy revisions and the implementation of more effective stewardship programs, both at the national and sub-national levels. Furthermore, ongoing research and surveillance will be essential in adapting these strategies to evolving trends in antimicrobial consumption and resistance.

Recommendations

Based on the analysis, the following recommendations are proposed:

- Strengthen Local Pharmaceutical Manufacturing: Implement targeted policies to support and enhance local pharmaceutical manufacturing capabilities. This will reduce dependency on imported antimicrobials and ensure a stable, reliable supply of essential medicines. Key actions could include providing incentives for local production, improving regulatory frameworks, and facilitating technology transfer.
- Revise the Ethiopian AWaRe Classification: Expand and update the Ethiopian AWaRe classification to include all antimicrobials consumed in the country. This will improve the accuracy of consumption monitoring and enable more effective stewardship efforts. Specific steps could include conducting a comprehensive review of current classifications and collaborating with international experts to ensure alignment with global standards.
- Enhance Surveillance and Data Collection Systems: Strengthen surveillance and reporting systems for AMC at the national, subnational, and health facility levels. Improving these systems will provide more accurate and timely data, aiding in the effective management of AMR. Actions could include investing in digital data collection tools, training healthcare professionals in data management, and establishing a centralized database for AMC and AMR data integration.
- Promote Rational Use of Antimicrobials: Develop and implement targeted education and stewardship programs to promote the rational use of antimicrobials. These programs should focus on educating healthcare providers and the public about the risks of antimicrobial misuse and the importance of adherence to treatment guidelines. Consider integrating these programs into existing healthcare training and public health initiatives.
- Integrate AMC Data with AMR Surveillance: Integrate AMC data with existing AMR surveillance systems to create a more comprehensive understanding of the relationship between antimicrobial use and resistance. This integration will enable more informed decision-making and policy development. Key actions could include aligning data collection methodologies, enhancing data-sharing protocols, and conducting joint analyses to identify trends and correlations.

Appendices

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