PHARMACOVIGILANCE
NEWSLETTER

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Consequences of AMR to Pharmacovigilance

Content

Health professionals and patients are encouraged to **report adverse events** or **quality problems** experienced with the use of **vaccines and medicines** to the nearest NAFDAC office or via pharmacovigilance@nafdac.gov.ng or via eReporting platform available on the NAFDAC website www.nafdac.gov.ng or via Med Safety Application available for download on Android and IOS stores.

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EDITOR'S NOTE...

We wish to thank our numerous stakeholders who have been working tirelessly with the National Pharmacovigilance Centre (NPC) to ensure the safe use of medicines in Nigeria. The NPC is committed to sending out the quarterly newsletter to its stakeholders. The objectives of the Newsletter are to disseminate information on Pharmacovigilance activities nationally and globally, to educate stakeholders on medicine safety issues, to promote rational use of drugs and to promote reporting of Adverse Drugs Reactions (ADRs) and AEFIs. This edition of the newsletter focuses on: **Consequences of AMR to Pharmacovigilance**

We encourage Health care Professionals and other stakeholders to continue to report all adverse drug reactions and AEFIs. Your valued comments and acknowledgement of receipt of this issue through our email addresses (pharmacovigilance@nafdac.gov.ng, fdic@nafdac.gov.ng) would be most appreciated.

Thank you for your relentless efforts in strengthening Pharmacovigilance System in Nigeria.

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Introduction

Antimicrobials refer to a broad range of medicines used to prevent and treat infections in humans, animals, and plants. They are designed to kill or inhibit the growth of microorganisms responsible for infections. However, with time antimicrobial resistance (AMR) occurs as microorganisms develop the ability to resist the antimicrobial action of previously effective medicines. Antibiotic resistance affects people of all ages in all countries. According to the World Health Organisation (WHO) Antimicrobial Resistance (AMR) occurs when bacteria, viruses, fungi and parasites no longer respond to antimicrobial agents. As a result of drug resistance, antibiotics and other antimicrobial agents become ineffective and infections become difficult or impossible to treat, increasing the risk of disease spread, severe illness and death. AMR is a threat to humans, animals, plants and the environment. (Anwar, M. et al, 2020). Yearly, an estimated 5.7 million deaths occur from treatable infectious diseases, mostly in low- and middle-income countries (LMICs), and many of these lives could have been saved if effective antibiotics were available. At the same time, there are about 700,000 annual deaths worldwide due to antibiotic resistance (Habarugira, J. M. V. et al, 2021).

Antimicrobial resistance (AMR) is one of the greatest threats to public health globally. It is primarily driven by the overuse and inappropriate utilization of antimicrobials. In Nigeria, AMR is exacerbated by the overuse of prescription-only medicines, including antimicrobials, without proper monitoring. Antimicrobial stewardship (AMS) in outpatient settings is a novel concept in Nigeria. The National Action Plan for Antimicrobial Resistance (2017-2022) highlighted widespread inappropriate antibiotic use, with significant proportions obtained without prescriptions (Adda D.K. et al, 2024). In 2019 alone, an estimated 4.95 million deaths associated with bacterial AMR was recorded; this is more deaths than caused by HIV/AIDS or malaria (Sharma, M. et al, 2021).

Consequences of Antimicrobial Resistance

Antimicrobial resistance (AMR) poses a significant global health threat, arising primarily from the misuse and overuse of antibiotics in both veterinary and public healthcare systems. The consequences of AMR are far reaching and severe. AMR leads to harder to treat infections, longer hospital stays, higher healthcare costs and increased deaths. Beyond its immediate health impact, AMR poses a serious threat to achieving the Sustainable Development Goals (SDGs).

Effectively addressing AMR requires collaboration among government, industry and the public sector to develop coordinated institutions and policies at all levels of regulation. SDG 17 focuses on partnerships for sustainable development; expanding this goal would facilitate global antimicrobial stewardship initiatives, technology transfer, surveillance systems, and investment in vaccine and drug research (Aslam, B. et al, 2024).

Antimicrobial stewardship and One health approach

AMR is a complex problem that requires both sector-specific actions in the human health, food production, animal and environmental sectors, and a coordinated approach across these sectors. One Health refers to an integrated, unifying approach that aims to achieve optimal and sustainable health outcomes for people, animals, and ecosystems. Indeed, it recognizes that the health of humans, domestic and wild animals, plants and the wider environment are closely linked and inter-dependent. The One Health approach to preventing and controlling AMR brings together stakeholders from relevant sectors to communicate and work together in the design, implementation and monitoring of programmes, policies, legislation, and research to mitigate AMR and attain better health and economic outcomes (WHO, 2023).

Antimicrobial stewardship involves coordinated efforts to promote the responsible use of antimicrobials, aiming to slow the development of resistance. It includes measures to optimize the choice of antibiotic, as well as the appropriate dose and duration of treatment. A good number of measures can be put in place to address AMR at hospital or country levels. As a program, antimicrobial stewardship is a set of interventions used to enhance the rational use of antibiotics. Various forms of antimicrobial stewardship programs have been established in different countries at different levels of care delivery with involvement of a wide range of stakeholders including clinicians, pharmacists, nurses and administrators and healthcare facilities (Habarugira, J. M. V. et al, 2021).

To promote appropriate use while maintaining access, the World Health Organization (WHO) introduced the AWaRe classification in 2017 as part of its Essential Medicines List (EML). This framework groups antibiotics into three categories *Access*, *Watch*, and *Reserve* (AWaRe) based on their indication, potential for resistance, and public health importance. A global campaign was launched in 2019, urging governments to implement the AWaRe tool through national guidelines to reduce antimicrobial resistance and ensure access. The AWaRe classification is a useful tool to be considered by monitoring activities targeting specific antibiotics (Habarugira, J. M. V. et al, 2021).

As the world puts in place various measures to curb the increasing threat of rising resistance to existing antibiotics, specific pharmacovigilance data could constitute an important part of the wider multi-disciplinary approaches used for resistance surveillance and warning.

Pharmacovigilance as a tool to monitor the rational use of antimicrobials

The spread of antimicrobial resistance (AMR) is a global challenge. Close and continuous surveillance for quick detection of AMR is difficult, especially in remote places. Pharmacovigilance (PV) is as an auxiliary tool

for identifying and monitoring the ineffectiveness, resistance, and inappropriate use of antibiotics (Sandes, V. et al, 2024). The following terms "drug ineffective", "therapeutic failure", "drug resistance", "pathogen resistance", and "multidrug resistance" are found in PV databases and dictionaries, denoting ineffectiveness. These terms cover a range of problems that require further investigation because they are useful warnings about possible cases of AMR. "Medication errors", especially those related to dose and indication, and "Off-label use" suggest inappropriate use of antibiotics. Pharmacovigilance is certainly a complementary tool for antimicrobial stewardship activities, especially in scenarios where other resources are scarce (Sandes, V. et al, 2024). Future research should explore how AMR-relevant MedDRA Terms are used in resource-limited settings with less capacity to generate laboratory-confirmed resistance data. (Habarugira, J. M. V. et al, 2021).

An analysis was conducted using data entered in VigiFlow between 1 January 2020 and 31 December 2024. The search focused on all antimicrobial medicines and applied specific terms to identify reports that may indicate lack of effectiveness or possible resistance. The following keywords were used: *"drug ineffective," "treatment failure," "drug resistance," "drug ineffective for unapproved indication,"* and *"suspected counterfeit product."*

OVERVIEW OF ANTIMICROBIAL REPORTS IN VIGILYZE (2020–2024)

Drug Categories Reported

Between 2020 and 2024, a total of **6,957** antimicrobial-related reports were retrieved from VigiLyze. The majority were associated with **antivirals for systemic use (65%)**, reflecting increased reporting during and after the COVID-19 pandemic. **Antimycobacterials (16%)**, mainly used for tuberculosis, were the next most frequently reported group. Other notable categories included **antibiotics and chemotherapeutics for dermatological use (7.3%)**, **sulfonamides and trimethoprim (5.9%)**, and **macrolides, lincosamides, and streptogramins (3.8%)**. Reports involving **antifungals** and **beta-lactam antibacterials** were comparatively fewer, each accounting for less than 3% of total reports.

This distribution suggests that monitoring efforts and reporting activity were greatest for medicines used in managing **viral and mycobacterial infections**, consistent with national and global health priorities in recent years.

Table 1: Drug Categories Reported

Drug (WHODrug)	Count	Percentage
ATC: D01 ANTIFUNGALS FOR DERMATOLOGICAL USE	66	1.0%
ATC: D06 ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	475	7.3%
ATC: J02 ANTIMYCOTICS FOR SYSTEMIC USE	66	1.0%
ATC: J04 ANTIMYCOBACTERIALS	1,033	16.0%
ATC: J05 ANTIVIRALS FOR SYSTEMIC USE	4,204	65.0%
ATC: J01A TETRACYCLINES	19	0.3%
ATC: J01B AMPHENICOLS	4	0.1%
ATC: J01C BETA-LACTAM ANTIBACTERIALS, PENICILLINS	143	2.2%
ATC: J01D OTHER BETA-LACTAM ANTIBACTERIALS	166	2.6%
ATC: J01E SULFONAMIDES AND TRIMETHOPRIM	383	5.9%
ATC: J01F MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS	248	3.8%
ATC: J01G AMINOGLYCOSIDE ANTIBACTERIALS	146	2.3%

Reports by Year

The number of antimicrobial-related reports fluctuated across the five years. The highest reporting occurred in **2021 (38.4%)**, likely linked to intensified pharmacovigilance efforts and increased antiviral use during the COVID-19 vaccination and treatment phases. Reporting declined in **2022 (20.5%)** and **2023 (13.0%)** before rising again in **2024 (18.6%).** The initial year, **2020**, accounted for **9.5%** of reports. The trend highlights how public health events and strengthened surveillance systems influence the volume of safety reports received over time.

Table 2: Reports by Year

YEAR	COUNT	PERCENTAGE
2020	615	9.5%
2021	2,485	38.4%
2022	1,325	20.5%
2023	839	13.0%
2024	1,204	18.6%

Frequency of Reported Preferred Terms

Reports linked to drug ineffectiveness were the most common, comprising 0.6% of total entries. Other terms such as treatment failure, drug resistance, drug ineffective for unapproved indication, and suspected counterfeit product were reported at very low frequencies (<0.1%). Although these proportions appear small, they provide valuable signals for identifying potential cases of antimicrobial resistance or reduced therapeutic response that may warrant further investigation.

Table 3: Frequency of Reported Preferred Terms (Meddra)

REPORTED PREFERRED TERMS (MEDDRA)	COUNT	PERCENTAGE
PT: DRUG INEFFECTIVE	36	0.6%
PT: TREATMENT FAILURE	5	0.1%
PT: DRUG RESISTANCE	3	0.0%
PT: DRUG INEFFECTIVE FOR UNAPPROVED INDICATION	1	0.0%
PT: SUSPECTED COUNTERFEIT PRODUCT	1	0.0%

Seriousness Criteria all antimicrobial-related reports

Among the reports analyzed, "other medically important conditions" accounted for the largest share (7.9%), followed by cases involving hospitalization (3.1%) and life-threatening reactions (2.1%). Reports of death (1.2%) and disability (1.7%) were less frequent, while congenital anomalies were rare (0.1%).

Overall, about 16% of all antimicrobial-related reports were classified as serious, underscoring the importance of ongoing vigilance and prompt follow-up for cases with significant health outcomes.

Table 4: Seriousness Criteria

Seriousness Criteria	Count	Percentage
Death	77	1.2%
Life Threatening	139	2.1%
Caused/Prolonged Hospitalization	202	3.1%
Disabling/Incapacitating	113	1.7%
Congenital Anomaly/Birth Defect	6	0.1%
Other Medically Important Condition	512	7.9%

Conclusion

Antimicrobial resistance (AMR) is one of the greatest threats to global public health primarily driven by the overuse and inappropriate utilization of antimicrobials. (Adda D.K. et al, 2024). The WHO AWaRe classification provides a valuable framework for monitoring and guiding the rational use of specific antibiotics (Habarugira, J. M. V. et al, 2021).

Addressing AMR requires urgent multidisciplinary solutions, and pharmacovigilance has the potential to strengthen existing AMR monitoring strategies. Pharmacovigilance databases offer critical insights into suspected resistance and inappropriate antimicrobial

use serving as a complementary data source alongside laboratory surveillance.

The findings from this analysis emphasize the continued importance of pharmacovigilance and antimicrobial stewardship. Strengthening surveillance at both hospital and community levels is essential to detect patterns of antimicrobial ineffectiveness early and to support evidence-based action against resistance.

Future research exploring how these AMR-relevant MedDRA terms are applied in resource-limited settings where laboratory-confirmed resistance data may be scarce will further enhance global understanding and response efforts (Habarugira, J. M. V. et al, 2021).

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