Review

ANNALS OF MEDICINE & SURGERY

OPEN

Revisiting the blind spot of substandard and fake drugs as drivers of antimicrobial resistance in LMICs

Bashar H. Gulumbe, BSc, MSc[a,*], Ridwan O. Adesola, DVM[b]

Abstract

One of the most significant risks to public health is ongoing antimicrobial resistance (AMR). Substandard and fraudulent medications, particularly in low- and middle-income countries (LMICs), are thought to have a role in the genesis and spread of AMR. There are numerous reports concerning the availability of subpar pharmaceuticals in developing countries, with no scientific evidence as to what exactly is included in some of the prescriptions supplied there. These counterfeit and inferior pharmaceuticals are a financial burden of up to US$200 billion, causing thousands of patient deaths, endangering both individual and public health,and undermining patient trust in the healthcare system. Poor quality and counterfeit antibiotics are often disregarded as possible causes of AMR in AMR studies. Therefore, we examined the issue of fake drugs in LMICs and its possible links to the emergence and spread of AMR.

Keywords: AMR, fake drugs, LMICs – substandard drugs, pathogens, resistance

Antimicrobial resistance (AMR) remains 1 of the biggest public health threats. Several factors are believed to contribute to the emergence and spread of AMR, including substandard and fake drugs, especially in low-income and middle-income countries (LMICs). The problem of substandard and falsified drugs continues to remain a significant public health challenge in these countries. There are several reports of the circulation of substandard medications in underdeveloped nations, but there is little analytical proof of what exactly is in some of the medicines sold there[1]. In 2017, a study by WHO reported that medical products in developing countries had a failure rate of 10.5%[2]. A year later, Ozawa *et al.*[3] reported a higher prevalence rate of 13.6% in the countries. Furthermore, in a recent survey conducted on the global prevalence of fake and substandard drugs by Zabala *et al.*[4], out of a total of 13,555 samples reviewed, up to 2,358.57, constituting 17.4% failed a minimum of 1 quality test. In addition, the authors revealed that out of the 10,137 articles examined in the survey, 648 were related to antibiotic quality and 116 (16.4%) were in LMICs. These fake and substandard drugs constitute an economic burden of up to US$200 billion and are responsible for the deaths of thousands of patients, pose a risk to both individual and public health, and erode patient confidence in the healthcare system[4]. When patients lose confidence in the healthcare system, they engage in self-medication, including buying antibiotics at the counter, contributing to the emergence of resistant strains.

The term 'falsified drugs' refers to drugs that deliberately/fraudulently mislead their identity, composition, or source, whereas authorized pharmaceuticals that do not meet their quality requirements, technical requirements, or both are considered substandard medications. These could be caused by egregious carelessness or unintentional mistakes made during the production process, or they might degrade as a result of improper storage or movement across the supply chain[4]. Substandard and falsified antibiotic medications with insufficient amounts of the active component can drive the development of AMR[5]. Suboptimal concentrations of antimicrobials can promote AMR for several reasons, including poor solubility, adulteration with subtherapeutic doses of unidentified, cryptic antibiotics, and substandard drugs[6]. For instance, the high incidence of poor-quality sulfamethoxazole–trimethoprim and chloramphenicol in Myanmar has been linked to the high prevalence of typhoid antibiotic resistance[7]. The kind of impact these drugs can cause gets even worst when they are not detected early.

Recently, at least 60 children died in the Gambia due to the consumption of low-quality cough syrup. The ugly event worries global health stakeholders, with WHO issuing a global alert over the 4 syrups on 5 October 2022, warning that they may be connected to acute renal damage and the deaths of children in the Gambia in July, August, and September[8]. Had these innocent children not died, the syrups would continue to circulate unnoticed. There are cases of low-quality antibiotics circulating without any immediately noticeable impact requiring an investigation[6]. This is 1 reason why the exact prevalence and impact of substandard and falsified antimicrobials are unknown in LMICs. Similarly, substandard and

[a]Department of Microbiology, Faculty of Science, Federal University, Birnin Kebbi, Kebbi State and [b]Department of Veterinary Medicine, Faculty of Veterinary Medicine, University of Ibadan, Ibadan, Oyo State, Nigeria

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Department of Microbiology, Faculty of Science, Federal University, Birnin Kebbi, Kebbi State 860231, Nigeria, Tel: +2347066287090 E-mail address: abashar.haruna@fubk.edu.ng (B. H. Gulumbe).

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Annals of Medicine & Surgery (2023) 85:122–123

Received 16 October 2022; Accepted 22 December 2022

Published online 7 February 2023

http://dx.doi.org/10.1097/MS9.0000000000000113

fake antibiotics are frequently overlooked as potential causes of AMR in AMR investigations.

There are various challenges that predispose to the usage of substandard and fake antibiotics in LMICs, which include methodological issues such as poor sampling techniques and analytical procedures, a lack of consensus regarding what constitutes a substandard or falsified medication, uneven geographic and therapeutic area coverage, and the scarcity of recent data. Additionally, poor regulatory frameworks and unmet market demands brought on by scarcity or high prices might open up a market for fake goods[9]. Similarly, purchasing medications online may increase the chance of getting a substandard product. Furthermore, most of the existing approaches to improving the quality of medications in LMICs concentrate on regulatory concerns. Still, the quality of medications is impacted by more prominent, system-wide reasons that offer commercial incentives.

To address the challenges, there is an urgent need for a system-wide approach that considers sociopolitical, economic, ethical, and public health aspects and involves stakeholders within and outside the national regulatory agencies[10]. Pharmacists have crucial roles in enhancing procurement procedures, educating and alerting patients to the dangers of buying medications from unreliable sources, and other related tasks. Increased knowledge on the part of pharmacists is necessary due to the weight of fake and substandard medications. Pharmacy education, by default, focuses on the quality of the manufacturing and usage of medications, despite the fact that training differs by country, area, and institution. To increase or reinforce professional knowledge among pharmacists, it is necessary to include compulsory modules that teach strategies and skills for recognizing and reporting substandard drugs.

In addition to educating pharmacists about fake drugs, some other essential programs and professionals may be targeted, such as Masters of Public Health students, professionals in the healthcare field, and community health workers on the ground. Here, governments should determine their educational needs and curriculum gaps in cooperation with professional groups, higher education institutions, and other pertinent stakeholders. A conversation on a global scale might inspire support and aid in setting standards for pharmacy education, and countries should create objectives and action plans for curriculum improvements that include checkpoints for measuring success[4,10]. Policymakers, on the other hand, should invest in the development and application of regulations to enhance fake drug detection and response and prohibit their entry and abuse. The significant instances of poor drug quality have adverse public effects and emphasize the importance of stringent drug laws in Africa.

As part of detection and prevention strategies, drug inspectors should access affordable screening tools for monitoring antibiotic quality. Prescribers and dispensers need to exercise greater caution, and those in charge of procurement should concentrate on their quality assurance services[4]. Thus, a coordinated effort motivated by vigilance and deontology is required. Finally, it is pertinent for AMR researchers to revisit the significant impact of substandard antibiotics on AMR spread in LMICs by looking at antibiotic quality epidemiology, which is poorly understood and neglected, and provide informed recommendations on how substandard antibiotics usage will be a story of the past in these countries.

Ethical approval

Not applicable.

Patient consent

Not applicable.

Sources of funding

None.

Author contribution

B.H.G. and R.O.A.: study concept, manuscript writing, review, and editing.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

B.H. Gulumbe.

References

[1] A study on the public health and socioeconomic impact of substandard and falsified medical products. World Health Organization; 2017.
[2] World Health Organization. 1 in 10 medical products in developing countries is substandard or falsified. Accessed 16, 2022. https://www.who.int/news/item/28-11-2017-1-in-10-medical-products-in-developing-countries-is-substandard-or-falsified
[3] Ozawa S, Evans DR, Bessias S, *et al*. Prevalence and estimated economic burden of substandard and falsified medicines in low- and middle-income countries: a systematic review and meta-analysis. JAMA Netw Open 2018;1:e181662.
[4] Zabala GA, Bellingham K, Vidhamaly V, *et al*. Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance? BMJ Global Health 2022;7:e008587.
[5] Kelesidis T, Falagas ME. Substandard/counterfeit antimicrobial drugs. Clin Microbiol Rev 2015;28:443–64.
[6] Taylor RB, Shakoor O, Behrens RH. Drug quality, a contributor to drug resistance? Lancet 1995;346:122.
[7] Shwe TN, Nyein MM, Yi W, *et al*. Blood culture isolates from children admitted to Medical Unit III, Yangon Children's Hospital, 1998. Southeast Asian J Trop Med Public Health 2002;33:764–1.
[8] World Health Organization. Medical Product Alert N°6/2022: substandard (contaminated) paediatric medicines. Accessed 14, 2022. https://www.who.int/news/item/05-10-2022-medical-product-alert-n-6-2022-substandard-(contaminated)-paediatric-medicines
[9] Pisani E, Nistor A-L, Hasnida A, *et al*. Identifying market risk for substandard and falsified medicines: an analytic framework based on qualitative research in China, Indonesia, Turkey and Romania. Wellcome Open Res 2019;4:70.
[10] Ferrario A, Orubu ESF, Adeyeye MC, *et al*. The need for comprehensive and multidisciplinary training in substandard and falsified medicines for pharmacists. BMJ Glob Health 2019;4:e001681.