Systematic Review – Knowledge, Attitudes and Practices of Healthcare Workers in Reporting Adverse Drug Reactions in Sub-Saharan Africa for Pharmacovigilance

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ABSTRACT

Introduction: This study aims to review the knowledge, attitude and practices of health care workers, including doctors, nurses, pharmacists and health officers in reporting adverse drug reactions (ADRs) for pharmacovigilance in sub-Saharan Africa

Methods: PubMed, Google Scholar and Trip databases were used to identify papers relevant for the review. Search results were narrowed down through a manual review of titles and abstracts based on inclusion criteria.

Results: There were 35 articles included in this review. It was found that generally, healthcare workers had inadequate knowledge regarding reporting of ADRs and pharmacovigilance. While private practice doctors have heard of pharmacovigilance and could define ADRs correctly, more than half did not know how or where to report them. The majority of healthcare workers had positive attitudes toward reporting ADRs. However, there was unwillingness in some settings due to concerns that it reflected poor clinical care on their part. All the studies identified consistently underreporting of ADRs admitted by healthcare workers.

Conclusion: While HCWs have positive attitudes regarding ADR reporting, there were significant knowledge deficits, particularly regarding how to report ADRs. This contributes to the under-reporting of ADRs, which may have implications for drug safety surveillance.

Keywords: Africa South of the Sahara; Drug-Related Side Effects and Adverse; Health Knowledge, Attitudes, Practice

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INTRODUCTION
An adverse drug reaction (ADR) is a “noxious and unintended” response from medicine when used at the normal dose “for prophylaxis, diagnosis or therapy of disease, or the modifications of physiological function”. [1] Adverse drug reactions from medications are a major concern for health policymakers, clinicians and patients because they impact treatment adherence, and increase healthcare costs, morbidity and mortality. ADRs may range from mild to life-threatening, with short or long-term effects. An ADR necessitates linkage or causality to that specific drug to be established.[2]

Monitoring for ADRs is especially important in Africa due to the prevalence of human immunodeficiency virus (HIV) infections and the use of antiretroviral (ARV) therapy. For example, in 2020, the prevalence rate of HIV infections in Eswatini is 27% among people aged 15 years and over.[3] This necessitated intervention and compliance with the 2030 Joint United Nations Programme on HIV/AIDS (UNAIDS) target of treatment coverage above 95% with ARV. This resulted in a significant decline of 44% in HIV incidence and a decline in AIDS-related mortality. [4] As ARVs have documented risks of ADRs and toxicity,[5] the high numbers of patients on these medications makes it necessary to systematically and consistently monitor their safety profiles through a robust pharmacovigilance system.

Pharmacovigilance can be achieved through a passive surveillance system based on voluntary and spontaneous reporting of ADRs, or active surveillance which entails deliberate and targeted monitoring through a pre-determined process.[6] When Eswatini utilised a passive system, ADR reporting rates were as low as 30 reports annually. An active surveillance system was established in 2013, focusing on patients on ARVs and anti-TB medicines, enrolling approximately 4300 patients over four years. This system required patients to be followed up for ADRs at each visit, resulting in approximately 400 ADRs reported annually. Further efforts to raise awareness on pharmacovigilance then led to the passive system receiving over 300 reports annually. While this demonstrates the feasibility to improve ADR reporting for drug safety monitoring, there is wide variation and under-reporting of ADRs. Although Africa has 69% of the world’s patients are on ARVs,[3] the continent accounts for only 6% of ADR reports from ARVs worldwide.[7]

Studies in Sub-Saharan Africa identified a lack of reporting knowledge, lack of information about national pharmacovigilance systems and absence of ADR identification and management knowledge as the leading causes of under-reporting ADRs.[8,9] ADR reporting helps to obtain detailed information on the safety profile of medicines and identify potentially avoidable ADRs, leading to reduced patient harm, and improved treatment outcomes.[6] This relies on healthcare workers (HCW) to identify and report ADRs, thus it is important to understand the knowledge, attitudes and practices (KAP) of HCW towards reporting ADRs. In this paper, the KAP of healthcare workers regarding ADR reporting in sub-Saharan Africa was reviewed.

METHODS
The research question was ‘What is Health Care Worker’s (HCW’s) KAP regarding reporting ADRs in sub-Saharan Africa?’. The PICO search strategy was used in its PIOT variation (as there was no comparator) to formulate the study question and set limits for the review. The population was healthcare workers including doctors, nurses, pharmacists and health officers in public and private healthcare facilities in sub-Saharan Africa. Intervention refers to knowledge, attitude and practices towards reporting adverse drug reactions; with expected outcomes being ADR reports from HCWs. The timeframe for research papers to be included was arbitrarily chosen between 2009 and 2020.
PubMed, Google Scholar and Trip databases were used for this literature review. For the PubMed search, MeSH terms used were “adverse drug reactions reporting systems” OR “drug-related side effects and adverse reactions” OR “pharmacovigilance,” AND “health personnel/education” AND “Africa south of the Sahara” AND “surveys and questionnaires”. Using the search builder, KAP was added to the search terms. These search terms were also used for Google Scholar. For the Trip database, the following PICO search was conducted: “P - healthcare workers in Africa”, “I – knowledge, attitudes, practices” and “O - ADR reports”. Search results were narrowed down through a manual review of titles and abstracts based on the inclusion criteria. The search for articles was initiated and completed in September 2020. Table 1 summarises the inclusion and exclusion criteria for this review.

<table>
<thead>
<tr>
<th>Studies included in the literature synthesis</th>
<th>Studies excluded from literature synthesis</th>
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<tbody>
<tr>
<td>KAP among healthcare workers</td>
<td>KAP of HCP unrelated to ADRs and PV (4)</td>
</tr>
<tr>
<td>Studies in Sub-Saharan Africa</td>
<td>Studies from other geographical regions (remainder) (2)</td>
</tr>
<tr>
<td>Studies conducted between 2009 - 2020</td>
<td>Studies from before 2009 (9)</td>
</tr>
<tr>
<td>Studies including ADRs associated with ARVs</td>
<td>Treatment guidelines and general systems reviews (7)</td>
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<tr>
<td>Mixed, quantitative and qualitative studies</td>
<td>Patient experience or patient opinion (3)</td>
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<tr>
<td></td>
<td>Pharmaceutics and therapeutics committee functionality and implementation of decisions (4)</td>
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The number of excluded articles based on exclusion criteria is indicated in brackets.

**RESULTS**

The PubMed search showed 912 hits, of which 41 were identified for inclusion. Google Scholar had 668 hits, of which 54 appeared suitable for screening. For the Trip database, the PICO search conducted had 259 hits with 2 articles included in the review. Figure 1 demonstrates the PRISMA flow diagram. There were 35 articles reviewed; the types of studies done are summarized in Table 2.

**Table 2: Types of Studies**

<table>
<thead>
<tr>
<th>Type of Study</th>
<th>Number Reviewed</th>
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<tbody>
<tr>
<td>Case-control study</td>
<td>1</td>
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<tr>
<td>Uncontrolled case study</td>
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<tr>
<td>Cohort analysis</td>
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<tr>
<td>Retrospective</td>
<td>5</td>
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<tr>
<td>Prospective</td>
<td>5</td>
</tr>
<tr>
<td>Systematic reviews</td>
<td>4</td>
</tr>
<tr>
<td>Cross-sectional study</td>
<td>16</td>
</tr>
<tr>
<td>Pre-post intervention study</td>
<td>2</td>
</tr>
<tr>
<td>Focus group discussion</td>
<td>1</td>
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</tbody>
</table>
Knowledge:
Generally, most of the studies found that HCWs had inadequate knowledge regarding ADR reporting and pharmacovigilance. A study based in a public Northeast Ethiopian hospital assessed nurses, midwives, doctors, pharmacists and health officers regarding ADR reporting. Among the respondents, 75.4% had inadequate knowledge regarding ADR reporting, with nurses and physicians reporting the lowest levels of pharmacovigilance knowledge. [8] Similarly, a cross-sectional study from Gondar, Ethiopia found only 53% had adequate knowledge of ADR reporting, with nurses and physicians reporting the lowest levels of pharmacovigilance knowledge. [10] In a South African provincial hospital, 83.7% of nurses and 65.4% of doctors responded incorrectly to the question regarding what constitutes an ADR.[11] A study of Kenyan hospitals found that while 42.8% of HCW had sufficient knowledge of ADR, only 24.7% knew about the national reporting system and associated guidelines. The majority had never seen the ADR form, while 71.1% did not know how to report ADRs. [12] Among community pharmacists from Lagos, Nigeria, 79% did not know the correct definition for an ADR, while 50.8% were not aware of pharmacovigilance centres and 22% admitted not receiving any pharmacovigilance training.[13] In Cameroon, 54% of the physicians were unaware of their national pharmacovigilance centre, while 10% of them had never heard of pharmacovigilance.[14] Among primary health care facilities from Southwest Nigeria, while 72.5% of HCW have heard of the pharmacovigilance centre, only 5.2% understood what it was for [15] A survey of doctors from Cote d’Ivoire identified that 71.7% did not know about the local
pharmacovigilance centre, with 83.2% never reporting ADRs to the national regulatory authority.[16]

This limited knowledge of reporting ADRs also extended to the private sector. Most doctors from a Nigerian private practice have heard of pharmacovigilance (82.9%), with 79.3% defining ADRs correctly. However, 56.2% did not know how to report ADRs or where to access these forms (71.7%).

Of six private hospitals from Gauteng, South Africa, 54.5% did not know how to report an ADR and 75.6% had never received pharmacovigilance training.[17]

**Attitudes:**
Generally, most HCWs had positive attitudes towards reporting ADRs. All community pharmacists in Harare surveyed believed reporting ADRs was very important and improves patient safety.[18] The majority of Lagos community pharmacists (90%) felt reporting ADRs should be mandatory for all HCWs.[13] Similarly, 86.3% of HCWs from Ethiopian health centres and 73.7% from Northeast Ethiopian hospitals had a positive attitude towards reporting ADRs.[8,10] In Kenya, 83.7% of respondents had a positive attitude towards ADR reporting and 86.7% felt that ADR reporting was their obligation.[12]

This positive attitude was also found in private practices. In Nigeria, the majority of the private doctors (89.6%) reported willingness to report ADRs if they were provided training.[16] A survey of nurses and pharmacists from private hospitals in South Africa found that 76% viewed pharmacovigilance as essential, with 87.1% agreeing that ADRs should be reported.[17]

However, there were several studies which found unfavourable attitudes toward ADR reporting. In Southwest Nigeria, only 46.2% HCWs had a favourable view regarding reporting ADRs.[15] In South Africa, 54.7% of nurses and 51.5% of doctors cited an unwillingness to report ADRs out of fear this would be attributed to poor clinical care on their part.[11] In Harare, it was also found that 38.6% HCWs were discouraged from reporting due to fear of professional liability.[18]

**Practices:**
The generally positive attitudes towards reporting ADRs do not necessarily equate to good practice. Studies consistently identified participants admitting to underreporting of ADRs. Of the community pharmacists in Lagos, only 30% had ever reported an ADR.

Of six private hospitals from South Africa, only 30% HCWs from South Nigeria teaching hospitals have reported ADRs, with 12.1% ever using the national reporting form. Most (93.2%) responded they would only report serious ADRs or those from new medications, compared to milder symptoms or those expected from the medications.[19] In Harare, although the pharmacists stated they manage up to five ADRs weekly, only 36.3% have ever reported ADRs.[18] Among HCWs from Sudan, 67% indicated they did not report ADRs due to a lack of awareness and knowledge regarding reporting.[20]

In Ethiopia, approximately half HCWs from health centres and northeast Ethiopian hospitals have never reported ADRs.[8,10] In Kenya, while 60.8% HCWs have been diagnosed with ADRs, only 21.7% have reported them formally.[12] In Cote D’Ivoire, only 14.8% of the ARV prescribers have reported ADRs.[16] A study from South Africa found that although 75% of nurses and 51.9% of the doctors had identified and managed an ADR at least once, only 6.7% had ever reported ADRs.[11] In Cameroon, a study identified only 4% of ADRs were reported to the national pharmacovigilance centre, while 90% were reported to medicine sales representatives.[14]

**DISCUSSION**
In this review, the KAP of HCWs in sub-Saharan countries on reporting ADRs was evaluated. The sub-Saharan countries were
grouped to obtain findings from similar healthcare systems, and demographic and socioeconomic settings. In addition, this region is of interest, due to the importance of pharmacovigilance with the high use of ARVs. Serious ADRs may necessitate treatment discontinuation, switches or substitutions, which may likely affect outcomes.[21] For example, in Eswatini, 76.7% of ARV regimen switches were due to ADRs, while in South Africa, ADRs from stavudine resulted in 74.1% of regimen switches.[22,23]

The main findings from these studies were that generally HCWs from sub-Saharan Africa have limited knowledge of pharmacovigilance activities, including how and where to report ADRs. While their attitudes are largely positive, the lack of knowledge appears to be a major barrier to ADR reporting. This was consistent with a study showing poor reporting rates were due to a lack of sufficient knowledge to identify ADRs, lack of healthcare provider confidence in handling ADRs and insufficient pharmacovigilance training for healthcare providers.[2] Although HCWs from the private sector were more knowledgeable about what ADRs were, the majority were still unaware of how and where to report ADRs. In terms of practice, most HCWs were not reporting ADRs despite identifying them during clinical encounters.

A study showed that previous areas of practice, academic qualifications and years of experience were significantly associated with ADR reporting practice.[17] Pharmacovigilance training and the introduction of active surveillance reporting were also shown to improve ADR reporting; which improved five-fold in public health facilities in Uganda. [24] However, another study showed that while HCWs receiving pharmacovigilance training had better theoretical knowledge and practice scores, it had a minimal overall impact on reporting rates. This suggests a need for sustained mentorship interventions to improve reporting rates.[25]

There is also a strong case for continuous training, quality assurance mentorship visits and the consistent presence of a pharmacovigilance focal person to promote the rate and quality of reporting. A study in Mpumalanga, South Africa, found that pharmacovigilance training and setting up committees improved ADR reporting rates.[26]

A study from an electronic ADR reporting system in Kenya identified additional issues that may affect pharmacovigilance practice. This study identified problems with infrastructure such as poor availability, reliability and access to the internet. Pharmacovigilance systems were unnecessarily complex with a hybrid system of paper and electronic reporting tools, as well as difficulty in navigating the electronic reporting system. The pharmacovigilance centre coordination was also affected by issues from this electronic system.[27]

Research Gap:
Limited studies were exploring the association between pharmacovigilance knowledge, attitudes and practice of ADR reporting. Facilitators and barriers to ADR reporting, including systems-related factors, require further investigation. The patient perspective on ADR reporting may also yield further findings that may have implications for pharmacovigilance.

CONCLUSION
This review identified that while HCWs have positive attitudes regarding ADR reporting, there were significant knowledge deficits, particularly regarding how to report ADRs. This contributes to the under-reporting of ADRs, which may have implications for drug safety surveillance. Understanding the KAP of HCWs helps to formulate strategies to strengthen ADR reporting and a sustainable, robust pharmacovigilance system.

CONFLICT OF INTEREST
None
SOURCE OF FUNDING
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REFERENCES
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