Brief communication

Adverse Drug Reaction Monitoring in Ethiopia: Analysis of case reports, 2002-2007

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Abstract

Background: Ensuring the health and safety of the public from adverse reaction of drugs is paramount. Adverse Drug Reactions Monitoring (ADRM) is a system that is put in place to ensure the health and safety of the public from adverse reactions of drugs. It heavily relies on health professionals (HPs) reporting of adverse events of drugs to drug regulators, in Ethiopia to the Drug Administration and Control Authority (DACA). The processed information, based on reported cases, is used to improve evidence based practice and underpins decisions to mitigate drug safety issues by drug regulators. However, the effectiveness of the ongoing ADRM system in Ethiopia in terms of its detection has never been evaluated.

Objective: To explore the magnitude of ADRM and suggest some practical improvement in Ethiopia.

Methods: The study analyzed the number of adverse drug reaction case reports received by DACA in a period of six years (2002 – 2007GC). All cases reported over the study period were included for analysis. Descriptive analysis was carried out to estimate the prevalence of adverse drug reactions and to assess their trend over the study period. To assess the strengths and weakness of the ongoing national ADRM, cases were analyzed by their location, time of occurrence, type of the health professional who made the case reports, drugs implicated, clinical manifestations and age of subjects affected.

Results: A total of 249 ADR cases were reported between 2002 and 2007. An average of 0.5 ADR cases per million populations were reported annually. The majority (36%) of all the cases were for 31 to 40 years of age. Cases were reported mainly (63%) from health facilities in the capital city. Physicians made 76% of all cases reported. Antiretroviral drugs were implicated in 70% of the cases reported. The most widely adverse events reported were dermatological disorders.

Conclusions: The level of ADR case reporting is very low showing the need to address major constraints of ongoing ADR monitoring. Thus, comprehensive measures aimed at improving under-reporting and effectiveness of ADRM should be instituted. [*Ethiop. J. Health Dev.* 2011;25(2):168-173]

Introduction

Lack of a system for monitoring drug safety is a major problem contributing to poor health in Ethiopia and other sub-Saharan countries. While demand for modern pharmaceuticals is increasing, parallel measures to ensure their safety are lacking (1-2).

It is known that different classes of adverse events might be displayed when drugs are exposed to different environmental and genetic influences (3-4). Studies have shown that the Ethiopian population has a distinct genetic makeup compared to Caucasian, Oriental or other Black populations (5). Monitoring the safety of these drugs contributes to building evidence on the safety of medicines pertinent to the Ethiopian population. ADRs increase morbidity, mortality and the cost of health care; however, ADR related morbidities are mostly avoidable (6-7). Monitoring ADRs helps reduce hospital admissions; and it saves substantial amount of financial and human resources which could be spent on patient treatment (9-11). It also contributes to detecting substandard and counterfeit medications (12-13).

A department for monitoring ADRs in Ethiopia was launched in 2002. However, little or no attempt was made to assess how the monitoring system functions in terms of ADR case detection and actions taken to improve it. We therefore assessed the patterns of ADR reporting to DACA from 2002 to 2007 GC and suggest some improvements in the ADRM system in Ethiopia.

Methods

Study design: This is a retrospective analysis of the national ADR case reports. DACA collects cases using adverse drug reactions reporting forms from public health facilities. As part of a routine, health professionals are expected to report cases with ADRs to DACA. The surveillance relies on voluntary spontaneous reporting of ADR cases by health professionals to DACA.

Data collection: For the purpose of this study, we took retrospective data of adverse drug reaction reports received by DACA during a period of six years (2002-2007GC).

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Study variables: This study included ADR reports on commonly used drugs in primary and secondary care including antitubercular, antiretrovirals, antifungals, antibiotics and analgesics.

Data analysis: Descriptive analysis was made using SPSS (version 12). Cases were analyzed based on: (i) their geographical area or location; (ii) their age group; (iii) time of occurrence; (iv) the health professional who reported cases (v) the drug implicated; and (vi) ADR manifestations. The prevalence of ADR was calculated for new cases with ADR per million population per year.

In relative terms, a large number of ADRs were received from the capital, Addis Ababa. Of the total cases detected, 156 (63%) were from the capital city while the remaining 82 (33%) were from other parts of the country.

Of the total reported ADR cases, 221 (95%) were in the age group 11 to 60 while 84 (36%) were between 31 to 40 years (Figure 1). There was no case report received for the age group less than one year.

The number of ADR cases reported to DACA has shown an increasing trend since 2002, with the exception of 2005 (Figure 2). A relatively marked increase in ADR

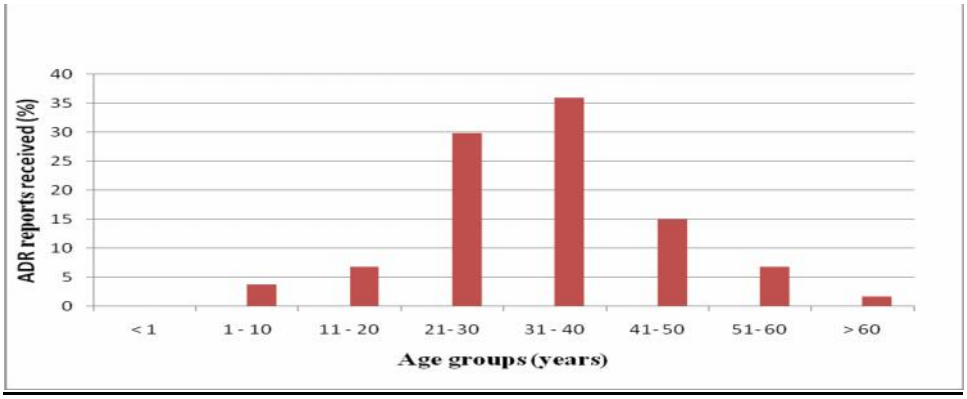

Figure 1: **Distribution of ADR case reports by their age group.**

The number of ADR cases reported to DACA has shown an increasing trend since 2002, with the exception of 2005 (Figure 2). A relatively marked increase in ADR reporting by HPs was recorded during the years 2006 and 2007.

Figure 3 depicts the proportion of ADR cases reported by types of health professionals. Most cases were detected and reported to DACA by physicians; 185 (76%). Druggists, pharmacy workforces who have a diploma qualification in pharmacy, detected 39 (16%) of the total cases. The remaining were reported by nurses and pharmacists.

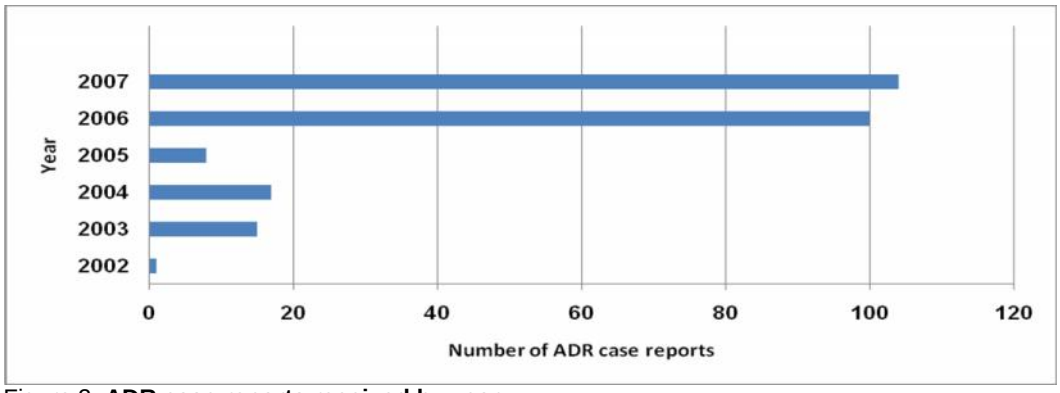

Figure 2: **ADR case reports received by year**

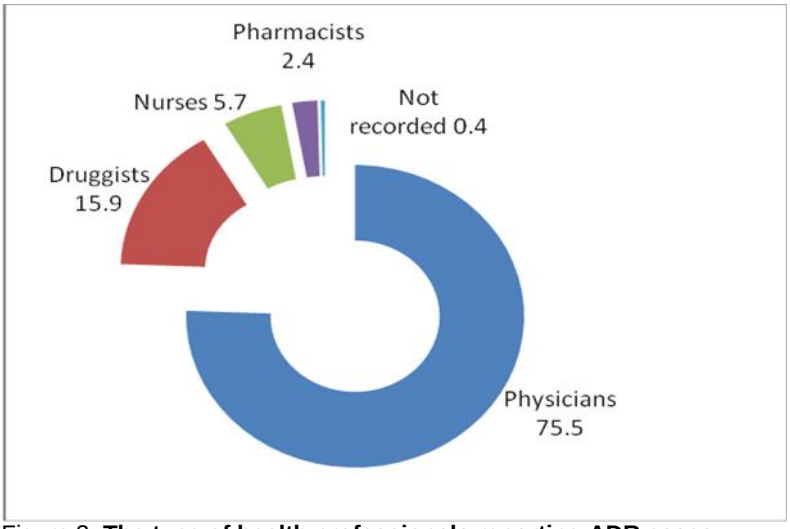

Figure 3: **The type of health professionals reporting ADR cases**

Table 1 shows the type of drugs implicated and the physiological systems affected by adverse events. Over 173 (70%) of ADR cases were reported for antiretroviral drugs, followed by antibiotics and anti-tubercular drugs. Reported manifestations of adverse events include dermatological 83 (34%), nervous system 70 (29%) and cardiovascular 36 (15%).

Table 1: **Drugs groups implicated for ADR and physiological systems affected**.

Drugs implicated	**Number of ADR case reports (%)**
Antiretrovirals	173(70.6)
Antibiotics	43(17.5)
Antituberculars	7(2.8)
Antifungals	6(2.4)
Analgesics	4(1.6)
System affected	
Dermatological system	83(34)
Nervous system	70(29)
Cardiovascular system	36(15)
Hepatic-portal system	16(7)
Metabolic system	15(6)
Gastrointestinal system	11(5)
Respiratory system	2(1)
No record	5(2)

Discussion

This study showed that the level of ADR under reporting is alarmingly low. The level of ADR monitoring is much higher in many other countries (14). The relatively low response of HPs outside the capital Addis Ababa could be attributed to a number of factors; namely poor access to medical information and lack of enough awareness and training programs. The high number of incomplete ADR case reports 11(4.5%) showed the low quality of the ADR reports.

There are no reports received for age groups under one and a small number of case reports were received for those who are 60 and over. Although the two groups are highly vulnerable to adverse events of drugs, the small number of ADR cases reports received shows the inadequate attention given to these groups. An increasing trend of ADR reporting to DACA were observed except in 2005. DACA's ADR awareness training programmes given to HPs for different HPs could be a factor in the relatively larger increase in ADR case reports received between 2006 and 2007. The main reason for decline in 2005 is not clear.

The low level of ADR reporting within the public health system could be attributed to several factors including poor quality of training of HPs, the unavailability of tools for reporting, low utilization and poor feedback on ADR surveillance reports and low coverage/poor integration at low health facilities. Several studies conducted in other countries support the importance of training HPs in improving under reporting of ADRs (15,16). Studies also report that training programs can help in changing attitudes towards reporting of very serious adverse events (17,18). These studies identified the need for tailoring educational programs towards attitudes which act as a barrier against ADR reporting. Up to now, no such studies were conducted that examined attitude and its effects on identification and reporting of ADRs in Ethiopia. Training methods, which employ other methods

like visual tools, such as using a videotape, have been found to have a greater impact than just oral presentation (19). This has been attributed to the graphic nature of educational videotapes.

Elsewhere, other reasons identified for under reporting by HPs included unavailability of reporting forms and the lack of information where to get one (20,21). Increasing the availability of ADR reporting forms within ADR bulletins and in prescription pads have been found to significantly increase ADR reporting (22). This was attributed to better convenience in obtaining ADR reporting forms at practice settings where they are required to be completed.

Involvement of all HPs is vital in improving under-reporting. Active ADR monitoring without the involvement of nurses is unlikely to achieve its purpose in Ethiopia. They are one of the key players in the health care system. Most of the lower health facilities in Ethiopia are staffed with nurses. The fact that nurses spend most of their time with patients is an asset in monitoring ADRs: this put them in a strategic position to detect ADRs. The involvement of nurses in the UK and Sweden has resulted in increasing ADR reports (23-24). Pharmacists and druggists can potentially contribute to ADR monitoring because of their availability in the rural parts of the country. The importance of embracing the multidisciplinary approach to improve under-reporting of ADRs need to be emphasized. Although there is evidence in favor of patient ADR reporting, this may be a less feasible option from the perspectives of cost and human resources (25).

One of the concerns of HPs about ADR reporting is not knowing what happened to the ADR report for that which they have made an effort and invested time to complete (26). Providing feedback to reporting institutions paves a path for further communication. It also builds trust within the system and helps to make a rapport with HPs. As such, feedback is indispensable interventions for encouraging more and further ADR reporting. They convey an impression that reports are taken seriously and are contributing towards improving the quality of drug safety (27-28). In addition to serving as a confirmation of ADR, receipt and appreciation of their effort in reporting, as each acknowledgment is given a reference number, it reduces double reporting of a single ADR.

In countries like Ethiopia, where HPs are under intense workload, the value of any motivational incentives cannot be ignored or undervalued. Lack of interest and motivation to report ADRs by HPs is one of the factors contributing to under reporting of ADRs. Providing incentives such as issuing a certificate for reporting ADRs or pens with a reminder logo as recognition for participation were shown to improve participation in ADR monitoring (29).

The introduction of antiretroviral drugs is quite recent in Ethiopia. Financial support gained through The President's Emergency Plan for AIDS Relief (PEPFAR) has made the availability of antiretroviral drugs a reality to thousands of patients (30). The fact that antiretroviral drugs, implicated in most ADRs received by DACA, shows the need for active pharmaco-vigilance system for newly licensed medicines in Ethiopia. A study done at St. Paul's Hospital in Addis Ababa has showed an increased risk of Nevirapine associated skin rash on HIV\AIDS female patients; and stressed the need for appropriate education for patients and HPs for the appropriate management of ADRs (31).

Most of these ADR cases reported to DACA were primarily based on direct clinical observations of patients. But, hematological adverse events which need laboratory results for accurate description of ADRs like agranolocytosis are not being reported to DACA. Blood disorders associated with the usage of drugs like oral chloramphenicol and dipyron injection are still widely practiced in Ethiopia. These drugs are still in use despite the fact that they had been banned from many countries because of their associated life threatening blood disorder (32, 33). Thus, harm caused by these drugs will still continue in Ethiopia unless surveillance and diagnostic capability of primary and secondary health facilities are improved.

Limitations

This study used retrospective case reports generated only in public health facilities. Consequently, the magnitude of ADR cases can be under-estimated because of exclusion of patients who consulted private practitioners over the study period. The other limitation is that the findings of the study may not reflect current status of cases with ADRs and its monitoring system. The study determined under-reporting of ADR cases and suggested ways to improve the problem. But, measures recommended need to be specified through more focused studies that explain the causes, concerns and difficulties faced by health professionals.

Conclusions

The level of ADR reporting is very low. In order to protect the public from avoidable adverse events, comprehensive intervention measures to improve under-reporting and effective surveillance should be instituted. These include training of HPs, ensuring the availability of reporting forms, encouraging the involvement of all HPs, providing feedbacks on ADR case reports and disseminating the findings of analysed case reports back to health care professionals where it underpins practice.

References

1. WHO. Country Health System Fact Sheet 2006 of Ethiopia. [Online]. Available from the World Wide Web: <http://www.who.int/countries/eth/eth/en/> [Accessed 30 September, 2008].

2. Embassy of India. 2006. Market survey on bulk drug and pharmaceutical products. [Online]. Embassy of India. Available from the World Wide Web: <http://cii.in/documents/market_africa.pdf> [Accessed 14 May, 2008].
3. Pirmohamed M**,** Atuah K, Dodoo A, Winstanley P. Pharmacovigilance in developing countries. British Medical Journal 2007; 335(7618):462.
4. Eliasson E. Ethnicity and adverse drug reactions. British Medical Journal 2006;332(7551): 1163-4.
5. Aklillu E, Persson I, Bertilsson L, Johansson I, Rodrigues F, Ingelman-Sundberg M. Frequent distribution of ultrarapid metabolizers of debrisoquine in an thiopian population carrying duplicated and multiduplicated functional CYP2D6 alleles. Journal of pharmacology and experimental therapeutics 1996;278(1):441-6.
6. Pirmohamed M, James S, Meakin S, Green C, Scott A, Walley T, Farrar K, Park B, Breckenridge A. Adverse drug reactions as cause of admission to hospital: Prospective analysis of 18,820 patients. British Medical Journal 2004;329(7456):15-9.
7. Lagnaoui R, Moore N, Fach J, Longy-Boursier M, and Begaud B. Adverse drug reactions in a department of systemic diseases-oriented internal medicine: Prevalence, incidence, direct costs and avoidability. European Journal of Clinical Pharmacology 2000;56(2):181-6.
8. Schlienger G, Oh I, Knowles R, Shear H. Quantifying the costs of serious adverse drug reactions to antiepileptic drugs. Epilepsia 39 Suppl 1998;7:27-32.
9. Dartnell G, Anderson P, Chohan V, Galbraith J, Lyon E, Nestor J, Moulds F. Hospitalisation for adverse events related to drug therapy: Incidence, avoidability and costs. The Medical Journal of Australia 1996;164(11):659-62.
10. Tribino G, Maldonado C. Direct costs and clinical aspects of adverse drug reactions in patients admitted to a level 3 hospital internal medicine ward. Biomedica 2006;26(1):31-41.
11. Vargas E, Terleira A, Hernando F, Perez E, Cordón C, Moreno A. and Portolés A. Effect of adverse drug reactions on length of stay in surgical intensive care units. Critical Care Medicine 2003;31(3):694-8.
12. Dodoo N, Renner L, van Grootheest C, Labadie J, Antwi-Agyei O, Hayibor S, Addison J, Pappoe V, Appiah-Danquah A. Safety monitoring of a new pentavalent vaccine in the expanded programme on immunisation in Ghana. Drug Safety 2007;30(4):347-56.
13. Akunyili N, Nnani C. Risk of medicines: Counterfeit drugs. International Journal of Risk and Safety in Medicines 2004;16(3):181-190.
14. WHO. Reporting to the WHO database.[Online]. Available from the World Wide Web : < http://www.who-umc.org/graphics/20635.jpg> [Accessed on 26 September, 2009].
15. Herdeiro T, Figueiras A, Polónia J, Gestal-Otero J. Improving the reporting of adverse drug reactions: a cluster-randomized trial among pharmacists in Portugal. Drug Safety 2008;31(4): 335-44.
16. Sweis D, Wong K. A Survey on factors that could affect adverse drug reaction reporting according to hospital pharmacists in Great Britain. Drug Safety 2000;23(2):165 -172.
17. Granas G, Buajordet M, Stenberg-Nilsen H, Harg P, Horn M. Pharmacists' attitudes towards the reporting of suspected adverse drug reactions in Norway. Pharmaco epidemiology and drug safety 2007;16(4):429-34.
18. Herdeiro T, Figueiras A, Polónia J. and Gestal-Otero J. Influence of pharmacists' attitudes on adverse drug reaction reporting: a case-control study in Portugal. Drug Safety 2006;29(4):331-40.
19. Morgan A, Frank J. Development of a videotape on adverse drug reactions. American Journal of Hospital Pharmacy 1990;47(6):1340-2.
20. Sebastian E. Adverse reactions to radiopharmaceuticals 1996 [Online]. Available from the World Wide Web: http://jnm.snmjournals.org/cgi/reprint/38/9/49N.pdf [Accessed 4 August, 2009]
21. Okezie O, Olufunmilayo F. Adverse drug reactions reporting by physicians in Ibadan, Nigeria." Pharmacoepidemiology and Drug Safety 2008;17(5):517-22.
22. Castel M, Figueras A, Pedrós C, Laporte R, Capellà D. Stimulating adverse drug reaction reporting: Effect of a drug safety bulletin and of including yellow cards in prescription pads. Drug Safety 2003;26(14):1049-55.
23. Hunt M, Gjoka G. Nurse reporting of adverse events caused by medicines. Nursing Times 2003;99(49):24-5.
24. Ulfvarson J, Mejyr S, Bergman U. Nurses are increasingly involved in pharmaco-vigilance in Sweden. Pharmaco-epidemiology and Drug Safety 2007;16(5):532-7.
25. Blenkinsopp A, Wilkie P, Wang M, Routledge A. Patient reporting of suspected adverse drug reactions. British Journal of Clinical Pharmacology 2006;63(2):148-156.
26. Juergens P, Szeinbach L, Janssen J, Brown R, Garner D. An evaluation of interventions designed to stimulate physician reporting of adverse drug events. Topics in hospital pharmacy management / Aspen Systems Corporation 1992;12(2):12-8.
27. Rao P, Archana B, Jose J. Implementation and results of an adverse drug reaction reporting program at an Indian teaching hospital. Indian Journal of Pharmacology 2006;38(4):293-294.
28. Wallerstedt S, Brunlof G, Marie-Louise, Tukukino C, Ny L. Reporting of adverse drug reactions may be influenced by feedback to the reporting doctor. European Journal of Clinical Pharmacology, 2007;63(5):505-8.

29. Vitillo J. Adverse drug reaction surveillance: practical methods for developing a successful monitoring program 2000. Medscape Pharmacists. [Online]. Available from the World Wide Web:<http://www.medscape.com/viewarticle/408575. [Accessed 18 June 18, 2008]

30. PEPFAR. Partners Working in Ethiopia (2008). [Online]. Available from World Wide Web: < http://www.pepfar.gov/countries/c19523.htm> Accessed [1 October, 2009]

31. Daniel A. Evaluation of ARV adverse drug reactions in adult HIV/AIDS patients taking ART.A retrospective study from St. Paul's Hospital, Ethiopia 2008;Unpublished.

32. Garcia S, Canionero M, Lopes G. Dipyrone-induced granulocytopenia: A case for awareness. Pharmacotherapy 2006;26(3):440-2.

33. Moorman J. Dipyrone (metamizole) use in the United States: a lethal tango? The Southern Medical Journal 2006;99(9):916.