Self-reported sulphonamide hypersensitivity reactions in adults living in Ibadan, Nigeria: A cross-sectional, community-based study

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ABSTRACT

Background: Documentation of adverse drug reactions (ADRs) is critical to a safe health delivery system. The aim of our study was to explore the prevalence of self-reported sulphonamide hypersensitivity reactions in a community-based sample of the general population in Ibadan, Nigeria. We also examined sociodemographic factors associated with ADRs in the sample. **Patients and Methods:** The study was cross-sectional in design with study sites in urban, semiurban, and rural settlement areas. Pretested questionnaires were administered on a one-on-one basis by trained interviewers. Frequency tables and percentages were computed for various levels of the variables. Chi-square test was used to assess the relationship between sulphonamide hypersensitivity and variables such as sociodemographic characteristics of respondents, respondents' knowledge of drugs, as well as drug sources. Variables found to be significantly associated with sulphonamide hypersensitivity were further investigated using multiple logistic regressions analysis. **Results:** Out of the 1062 respondents, 15.5% reported hypersensitivity to sulphonamides with skin reactions being the most prevalent. The proportion reporting ADRs was significantly higher among respondents with tertiary education (23.1%) than any other level of education (P = 0.008). In addition, individuals who were very knowledgeable about drug use (odds ratio [OR]: 2.07; 95% confidence interval [CI]: 1.15–3.73) and persons who got drugs from hospitals (OR: 2.00; 95% CI: 1.10–3.65) were more likely to report ADRs than those who were ignorant about drugs and those who purchased drugs from open markets, respectively. **Conclusion:** Prevalence of sulphonamide hypersensitivity is high among respondents, and ADRs is likely to be reported by people who are knowledgeable about drug use.

Key words: Adverse drug reaction, drug sourcing outlets, skin reactions, sulphonamide hypersensitivity

INTRODUCTION

Adverse drug reaction (ADR) is defined as a response to a medicine, which is noxious, unwanted or harmful, and unintended, and which occurs at doses normally used in human for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function.[1] Incidences of adverse reactions to drugs are widespread across populations and globally, vaccines and antibiotics are among the leading causes of these reactions.[2-5] In addition to antibiotics, herbal medicines and antimalarial drugs have contributed significantly to ADRs in Nigeria.[2] Although developed countries have established monitoring systems that readily identify, report, and rapidly respond to

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ADR, it is not so in some developing countries like Nigeria, where data on the prevalence of adverse reactions to drugs in the population still is scanty.[6,7]

Studies have established the occurrence of sulphonamide-induced hypersensitivity reactions when used,[8-10] and among antibiotics, sulphonamides have been reported to have a higher prevalence of adverse reactions.[11,12] These sulphonamide hypersensitivity reactions are majorly dermatological in expressions such as pruritus, fixed drug eruptions, maculopapular rash, and the life-threatening Steven–Johnson syndrome.[13,14]

Acquisition of epidemiologic data can supply information concerning the prevalence of drug hypersensitivity. Being a female, presence of concomitant infections (HIV, herpes), self-medications, and concurrent illnesses (systemic lupus erythematosus) have been identified as significant risk factors[14,15] in some populations. In resource-poor economies, other predictive factors could be significant in supplying similar information. Such factors could include economic status of the individual, educational exposure, and drug purchasing outlets.[7]

Studies on identification and documentation of ADRs have majorly been carried out either in hospitalized patients, among medical health professionals, students undergoing one form of medical training or within university communities.[2,7,13,16] Very little information exists on ADRs identification and/or reporting among semiurban and/or rural communities, and among individuals who are relatively educationally disadvantaged (illiterates).[17] This study which was carried out in study sites across urban, semi-urban, and rural lifestyles was with the objective of determining the prevalence of sulphonamide hypersensitivity and associated sociodemographic factors within a subpopulation in Nigeria; a country where the practice of self-medication is still high and where control over prescription medicines (such as sulphonamides) is still slack.[16,18]

SUBJECTS AND METHODS

The study (protocol number UI/EC/10/0021) was approved by the University of Ibadan/University College Hospital Institutional Review Board. Participants were made to understand that participating in the study was voluntary. Confidentially of data was ensured as interviews were conducted privately and only participants who gave informed consents were interviewed. Participants signed a written consent to participate in the study, accompanied with an introductory letter that was in accordance with the Declaration of Helsinki.

The study design was cross-sectional with participants selected from three residential categories: Urban, semiurban, and rural settlements within Ido local government area in Ibadan metropolis.

Participants for this study were adult residents drawn from different communities, educational levels, and works of life. For effective community entry, the services of a trained community mobilizer from the Department of Public Health, College of Medicine, UI, was employed. In the urban areas, mobilization of eligible participants for the study was via the Landlord Associations of the selected residential areas while at the semi-urban and rural areas, mobilization was through the local chiefs and their governing council.

A structured questionnaire was designed and pretested in two separate groups of 20 persons each tested twice within a space of 2 weeks apart. The questionnaire consisted of questions on observed sulphonamide hypersensitivity reactions (such as itching, skin rash or hives [urticaria], scaling and/or peeling of the skin, joint pain, changes in vision, difficulty in movement, redness of skin or lips, fever, difficulty in breathing, or sore throat, following drug intake without any other reason), the name of the culprit drug, and time and duration of the reaction. It also included questions on knowledge of the respondent's familiarity with drugs and their usage, drug purchasing sources, and mode of obtaining prescriptions. Response to history of previous reaction to sulphonamides was based on participants self-report. The period of recall of ingestion of sulphonamides was limited to 2 months prior to the study period. The questionnaires also contained demographic information as well as additional data on the educational status, monthly income, and current employment status.

The questionnaire was administered by trained interviewers and every interview was conducted on a one-on-one basis to ensure confidentiality. Moreover, samples of the drugs (both branded and generics) were shown to respondents to ease recognition. For respondents who could not communicate effectively in English language, questionnaires translated into the local language, Yoruba, were administered.

Responses were coded, entered into a computer, and doubled checked to ensure completeness and consistency. The entire dataset was checked for outlier responses and inconsistencies of information. Some questionnaire items containing too many responses were re-coded into meaningful groups appropriate for the type of analysis performed. Frequency tables and percentages were computed for the various levels of the variables. Chi-square test was used to assess the association of sulphonamide hypersensitivity with sociodemographic characteristics of the participants, participant's knowledge of drugs, and sources of drugs. Variables found to be significantly associated with ADRs were further investigated using multiple logistic regressions analysis. All analyses were performed at 95% level of significance using the Statistical Package for Social Science (SPSS) version 20. (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY).

RESULTS

Majority of the respondents (62.9%) were females while 37.1% of them were males [Table 1]. Although <6% of the study population were teenagers, majority of them (57.3%) were <40 years old. More than 80% of the respondents had at least primary education while <20% of them reported that they had no formal education.

Ignorance of drug knowledge was high with more than half (63.3%) of the respondents acknowledging that they had little information on proper drug usage and administration [Table 2]. Given a memory recall time frame of not more than 2 months prior to the study time, it was observed that use of antibiotics (40.1%) and antimalarial drugs (45.7%) were common among participants. Common classes of antibiotics used included sulphonamides, penicillins, and fluoroquinolones while the antimalarials having the artemisinin combinations therapies ranked highest. Sulphonamide-containing antimalarial drugs (13.9%) were also commonly used.

Furthermore, although most (43.3%) of the respondents reported that they obtained their drugs from

Table 1: Sociodemographic characteristics of respondents

Variables	Frequency (%)
Sex	
Male	394 (37.1)
Female	668 (62.9)
Age (years)	
<20	59 (5.6)
20-39	608 (57.3)
40-59	275 (25.9)
≥60	120 (11.3)
Employment status	
Employed	231 (21.8)
Unemployed	50 (4.7)
Self-employed	416 (39.2)
Student	281 (26.5)
Others*	32 (3.0)
No response	52 (4.9)
Highest level of education	
No formal education	171 (16.1)
Primary school	174 (16.4)
Secondary school	245 (23.1)
Tertiary school	472 (44.4)
Marital status	
Never married	379 (35.7)
Married	567 (53.4)
Previously married	116 (10.9)
Ethnic background	
Yoruba	860 (81.0)
Igbo	74 (7.0)
Hausa	11 (1.0)
Others	117 (11.0)

*Others include retirees, homemakers, and arts and design

Table 2: Knowledge of drugs, sources, and side effects

Variables	Frequency (%)
How much information do you have about drugs used for the treatment of illnesses?	n=1062
I am very knowledgeable about drugs and their use	100 (9.4)
I am fairly knowledgeable about drugs and their use	252 (23.7)
I am ignorant on drug use	672 (63.3)
Uncertain	38 (3.6)
How do you source for your drugs?	
Purchase from pharmacies	292 (27.5)
Given at the hospital/clinic	460 (43.3)
Purchase from the open market/patent medicine store	248 (23.4)
Can't remember	62 (5.8)
Have you used any antibiotics in the last 2 months?	
Yes	426 (40.1)
No	616 (58.0)
Can't remember	20 (1.9)
Which antibiotics did you use first?	
Sulphonamides	181 (17.0)
Penicillins	139 (13.1)
Fluoroquinolones	34 (3.2)
Cannot remember	708 (66.7)
Which antibiotics did you use again?	
Sulphonamides	25 (2.4)
Penicillins	49 (4.6)
Fluoroquinolones	18 (1.7)
Can't remember	970 (91.3)
Have you used any antimalarial in the last 2 months?	
Yes	485 (45.7)
No	560 (52.7)
Can't remember	17 (1.6)
If yes, which antimalarial did you use?	
Fansidar	148 (13.9)
ACTs	174 (16.4)
Chloroquine	75 (7.1)
Cannot remember	665 (62.6)
Have you ever experienced any side effect as a result of taking these drugs (mentioned above)?	
Yes	165 (15.5)
No	811 (76.4)
Can't remember	86 (8.1)
Which of the following features was the one most severe problem you had after taking the drug?	n=165
Skin reactions	97 (58.8)
Fever	52 (31.5)
Can't remember	16 (9.7)
Were you admitted in the hospital as a result of these symptoms?	
Yes	7 (4.2)
No	127 (77.0)
Can't remember	31 (18.8)
Did this reaction disappear when you stopped using the drug?	
Yes	107 (64.8)
No	11 (6.7)
Can't remember	47 (28.5)
Have you ever used the drug again?	
Yes	38 (23.0)
No	120 (72.7)
Can't remember	7 (4.2)

ACTs – Artemisinin combinations therapies

hospitals/clinics, many (23.4%) still confessed to have purchased their drugs from the open market/patent medicine store. Overall, 15.5% of the participants reported to have experienced ADRs to sulphonamide drugs. In Figure 1, skin reactions were the predominant ADRs experienced by most participants irrespective of the type of antibiotics used. However, most of those who used sulphonamides were respondents who admitted to be ignorant of drugs and drug use while the majority of those who used penicillins and fluoroquinolones were respondents who claimed to be very knowledgeable about drugs [Figure 2].

In Table 3, the proportion of the study participants reporting ADRs was significantly higher among respondents with tertiary education (23.1%) than any other level of education (*P* = 0.008). In addition, the proportion of the study participants reporting ADRs was significantly higher among those who claimed to be knowledgeable about drugs (27%, *P* < 0.001).

For the adjusted logistic regression [Table 4], the odds of reporting ADRs to sulphonamides was lower among respondents who had primary (odds ratio [OR]: 0.42; 95% confidence interval [CI]: 0.20–0.88) and secondary (OR: 0.43; 95% CI: 024–0.78) education compared to respondents with tertiary education. On the other hand, the odds of reporting ADRs to sulphonamides were higher among individuals who were very knowledgeable about drug use (OR: 2.07; 95% CI: 1.15–3.73), and persons who got drugs from hospitals (OR: 2.00; 95% CI: 1.10–3.65) compared to those who were ignorant about drugs and those who purchased drugs from open markets, respectively [Table 4].

DISCUSSION

This study investigated the prevalence of self-reported sulphonamide hypersensitivity in respondent residents across urban, semiurban, and rural communities in Ido local government area, Ibadan, Nigeria. Although most ADRs studies are clinic/hospital based, this community-based

Table 3: Investigating factors associated with drugs side effect using Chi-square test

Variables	Side effect of drugs		P
	Yes	χ^2	
Sex			
Male	54 (13.7)	1.08	0.30
Female	111 (16.6)		
Age (years)			
<20	6 (10.2)	2.48	0.48
20-39	100 (16.4)		
40-59	45 (16.4)		
≥60	14 (11.7)		
Employment status			
Employed	37 (16.0)	24.74*	<0.001
Unemployed	7 (14.0)		
Self-employed	41 (9.9)		
Student	63 (22.4)		
Others	9 (28.1)		
Highest level of education			
No formal education	16 (9.4)	36.44*	0.008
Primary school	16 (9.2)		
Secondary school	24 (9.8)		
Tertiary school	109 (23.1)		
Ethnic background			
Yoruba	119 (13.8)	11.78*	0.008
Igbo	17 (23.0)		
Hausa	3 (27.3)		
Others	26 (22.2)		
How much information do you have about drugs used for the treatment of illnesses?			
I am very knowledgeable about drugs and their use	27 (27.0)	27.27*	<0.001
I am fairly knowledgeable about drugs and their use	57 (22.6)		
I am ignorant on drug use	75 (11.2)		
How do you source for your drugs?			
Purchase from pharmacies	61 (20.9)	14.82*	0.001
Given at the hospital/clinic	78 (17.0)		
Purchase from the open market/ patent medicine store	19 (7.7)		
Which antibiotics did you use?			
Sulphonamides	20 (11.0)	4.82	0.09
Penicillins	27 (19.4)		
Fluoroquinolones	6 (17.6)		

Note: Analysis excluded missing observations. *P >0.05
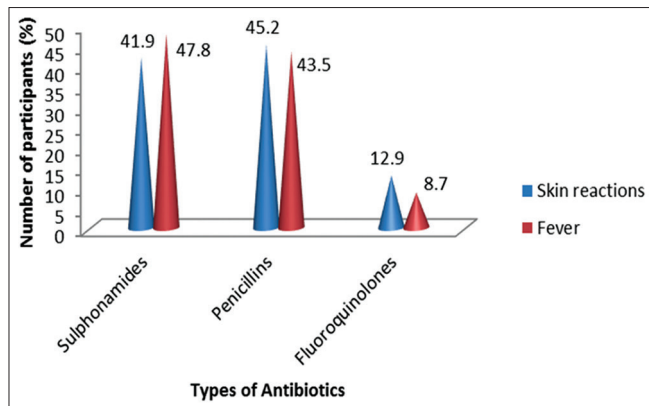
Figure 1: Adverse drug reactions among participants using different antibiotics
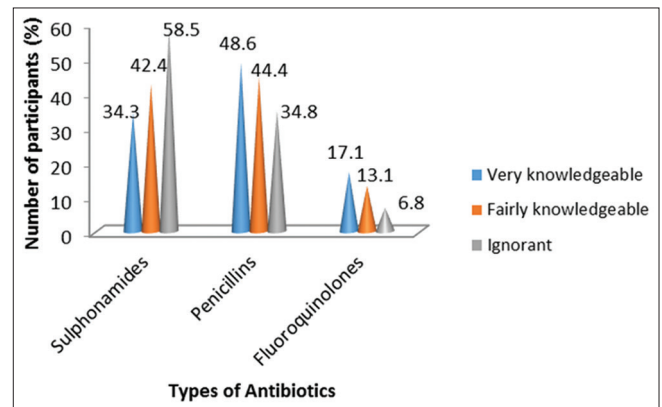
Figure 2: Participants' level of drug knowledge and use of antibiotics

Table 4: Evaluating the likelihood of experiencing drug side effects among participants

Variables	Odds of experiencing drugs side effects					
	Unadjusted analysis		P	Adjusted analysis		P
	OR	95% CI for OR		OR	95% CI for OR	
Employment status						
Employed	0.48	0.20-1.13	0.09	0.26	0.10-0.67	0.006
Unemployed	0.40	0.13-1.23	0.11	0.28	0.08-0.94	0.04
Self-employed	0.27	0.11-0.63	0.002	0.28	0.11-0.72	0.008
Student	0.71	0.31-1.65	0.43	0.33	0.13-0.85	0.02
Others	-	-	-	-	-	-
Highest level of education						
No formal education	0.37	0.21-0.65	0.001	0.49	0.22-1.09	0.08
Primary school	0.33	0.19-0.59	<0.001	0.42	0.20-0.88	0.02
Secondary school	0.35	0.22-0.56	<0.001	0.43	0.24-0.78	0.005
Tertiary school	-	-	-	-	-	-
Ethnic background						
Igbo	1.93	1.08-3.47	0.03	1.57	0.81-3.06	0.19
Hausa	2.13	0.56-8.16	0.27	2.01	0.47-8.62	0.35
Others (Edo, Igbira, Tiv)	1.95	1.20-3.16	0.007	1.65	0.95-2.86	0.08
Yoruba	-	-	-	-	-	-
How much information do you have about drugs used for the treatment of illnesses?						
I am very knowledgeable about drugs and their use	2.91	1.75-4.85	<0.001	2.07	1.15-3.73	0.02
I am fairly knowledgeable about drugs and their use	2.24	1.53-3.29	<0.001	1.58	1.00-2.48	0.048
I am ignorant on drug use	-	-	-	-	-	-
How do you source for your drugs?						
I purchased it from a pharmacy	2.87	1.65-4.97	<0.001	2.00	1.10-3.65	0.02
I was given at the hospital/clinic	2.21	1.30-3.77	0.003	2.15	1.22-3.79	0.008
I purchased it from the open market/patent medicine store	-	-	-	-	-	-

CI – Confidence interval; OR – Odds ratio

study contributes unique information on the prevalence of sulphonamide hypersensitivity in the studied populations.

Important in our study is the high prevalence of sulphonamide hypersensitivity which is over 5 times what is reported for healthy Caucasian populations[19] and a quarter of what obtains in HIV/AIDS patients.[20] This reveals a marked difference between our African (Nigerian) population and Caucasians, possibly serving as a pointer for evidence-based treatment of concurrent diseases in the studied populations.

It was observed that despite increased bacterial resistance to sulphonamides and availability of effective alternatives which over time have narrowed the use of sulphonamides as first-line treatments for infections, the drugs are still highly used in Nigeria. Likely factors encouraging the increased use of sulphonamides within the Nigerian healthcare system could be the use of outdated treatment guidelines, high cost of pharmaceutical alternatives to sulphonamides, and restricted access to these alternatives. Accessibility to alternative drugs is restricted because they are mostly available in registered pharmacies and cannot be purchased without a valid prescription.[20,21] This relatively high incidence of sulphonamide hypersensitivity, possibly calls for a need to review our current drug policies so that drugs that are potential candidates for ADRs are

either discontinued for better options or banned from use.[22]

Sulphonamides are employed as anti-infectives, and although they are meant to be prescription-only-medications (POM), they can readily be purchased as an over-the-counter medication in Nigeria. This makes them prime targets for drug misuse and/or abuse.[21] Patronage of open drug markets or patent medicine stores for POM is undoubtedly high as attested to from the results obtained in this study. The attendant danger with this is increased opportunities for circulation of counterfeit/fake/substandard drugs which are candidates for drug toxicities *in vivo*, leading to ADRs in unsuspecting individuals.[23] Unfortunately, drug handlers at the level of patent medicine stores and/ or open drug markets lack the professional expertise required for proper identification, distribution, storage, and dispensing of medications. The drug regulatory authority in the nation - National Agency for Food Drug, Administration and Control (NAFDAC) - continues to invest much into public enlightenment on safe use of drugs which has helped to reduce the circulation of counterfeit drugs by over 80% from what it was in 2001.[21] However, much still needs to be done to safeguard the populace from patronising unregistered drug sources, most especially for POMs. We found that education (level of literacy) informs people's cognisance of incidences of ADRs in their drug

usage. In particular, we observed that participants who had no formal education, only primary education, and those who had secondary education were less likely to report the incidence of ADRs than those who have tertiary education. Most tertiary institutions in Nigeria run a general studies program that encompasses topics across all disciplines such that graduates have basic information in all spheres of life. One of such topics is on drugs and its use in mankind, which gives a general overview necessary to raise awareness in individuals about ADRs.[24] Such level of awareness/education could be responsible for the majority of the reported cases of ADRs among individuals with tertiary education.

Underreporting of ADRs in health institutions in Nigeria is still an issue[25-27] probably because poor knowledge of drugs and their uses may account for individuals not being pharmacovigilant enough to recognize an undesired effect as a drug-induced adverse effect and so may not report it.[19] It is advantageous for individuals to recognize drugs they respond adversely to and so avoid them, but the possibility of re-exposure to the same drugs without relating the adverse effects suffered is very high.[19] To this end, the National Pharmacovigilance Centre was instituted by NAFDAC to educate stakeholders on drug safety issues, promote rational use of drugs, and to promote spontaneous reporting of ADRs to appropriate health authorities. Unfortunately, data on the efficiency of these activities in the general population is unavailable. In our study, it is surprising to note that a significant proportion of those who suffered an ADRs after taking a sulphonamide still repeated the intake of the drug at some later time.

Being economically buoyant guarantees increase in purchasing strength, especially if the desired product is available and affordable. These properties (availability and affordability) of sulphonamides, coupled with their efficacy in the treatment of infectious diseases possibly accounts for the strong association between employment status and sulphonamide hypersensitivity. A higher percentage of the study population is employed and (most sulphonamide drugs sell for <$2) so can afford the drug and are therefore more exposed to experiencing ADR.

Limitations of the study
A major limitation of this study is the fact that ADRs was self-reported. Although we admit that physician-reported ADRs information may provide professional data, many ADRs occurring at the community level in these settings often go unreported due to both unawareness and lack of access to well-structured health reporting systems. In addition, the study sites selected were predominantly occupied by Yorubas. A study in locations with fairly uniform ethnic distributions would have provided clearer ethnic/cultural dimensions to ADR. Some unpredictable

selection or recall biases might have also affected the generalizability of our findings; respondents possibly might have thought of some symptoms as being insignificant or irrelevant to the study objectives. Although we limited recall period to not more than 2 months before the study time and also took along many sample packs of the culprit drugs, reports in cross-sectional studies are known to largely depend on the accuracy of the respondents. Notwithstanding, adequate efforts were made to present accurate and comprehensive reports in this study sufficient as a scientific evidence to inform policy and further study directions on the subject.

CONCLUSION

Sulphonamide hypersensitivity is high in the studied population. Purchasing of drugs from the open market, level of literacy, ethnicity, and knowledge of drug use are factors associated with ADRs to sulphonamides in the studied area. In obtaining a complete ADRs information, a community-wide investigation should be built into ADRs surveillance activities.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Definitions – Definitions.pdf. WHO. Available from: http://www.who.int/medicines/areas/quality_safety/safety_efficacy/trainingcourses/definitions.pdf. [Last cited on 2014 May 07].
2. Oshikoya KA, Njokanma OF, Chukwura HA, Ojo IO. Adverse Drug Reactions in Nigerian Children – 8_2_s7.pdf. Paediatric and Perinatal Drug Therapy; 2007. p. 81-8. Available from: http://www.group.bmj.com/docs/pdf/8_2_s7.pdf. [Last cited on 2014 May 03].
3. Weiss J, Krebs S, Hoffmann C, Werner U, Neubert A, Brune K, *et al.* Survey of adverse drug reactions on a pediatric ward: A strategy for early and detailed detection. Pediatrics 2002;110 (2 Pt 1):254-7.
4. Impicciatore P, Choonara I, Clarkson A, Provasi D, Pandolfini C, Bonati M. Incidence of adverse drug reactions in paediatric in/out-patients: A systematic review and meta-analysis of prospective studies. Br J Clin Pharmacol 2001;52:77-83.
5. Fattahi F, Pourpak Z, Moin M, Kazemnejad A, Khotaei GT, Mamishi S, *et al.* Adverse drug reactions in hospitalized children in a department of infectious diseases. J Clin Pharmacol 2005;45:1313-8.
6. Kurt E, Demir AU, Cadirci O, Yildirim H, Pinar Eser T. Immediate-type drug hypersensitivity and associated factors in a general population. Allergol Immunopathol (Madr) 2011;39:27-31.
7. Lunet N, Falcão H, Sousa M, Bay N, Barros H. Self-reported food and drug allergy in Maputo, Mozambique. Public Health 2005;119:587-9.
8. Lau G, Kwan C, Chong SM. The 3-week sulphasalazine syndrome strikes again. Forensic Sci Int 2001;122:79-84.

9. Strom BL, Schinnar R, Apter AJ, Margolis DJ, Lautenbach E, Hennessy S, *et al.* Absence of cross-reactivity between sulfonamide antibiotics and sulfonamide nonantibiotics. N Engl J Med 2003;349:1628-35.
10. Rieder MJ, Shear NH, Kanee A, Tang BK, Spielberg SP. Prominence of slow acetylator phenotype among patients with sulfonamide hypersensitivity reactions. Clin Pharmacol Ther 1991;49:13-7.
11. Macy E, Poon K-Y T. Self-reported antibiotic allergy incidence and prevalence: Age and sex effects. Am J Med 2009;122:778.e1-7.
12. Lutomski DM, Lafollette JA, Biaglow MA, Haglund LA. Antibiotic allergies in the medical record: Effect on drug selection and assessment of validity. Pharmacotherapy 2008;28:1348-53.
13. Ensina LF, Amigo MH, Koch T, Guzman E, Paoli R, Nunes IC. Drug hypersensitivity in students from São Paulo, Brazil. Clinics (Sao Paulo) 2010;65:1009-11.
14. Warrington R, Silviu-Dan F. Drug allergy. Allergy Asthma Clin Immunol 2011;7 Suppl 1:S10.
15. Guglielmi L, Guglielmi P, Demoly P. Drug hypersensitivity: Epidemiology and risk factors. Curr Pharm Des 2006;12:3309-12.
16. Abasiubong F, Bassey EA, Udobang JA, Akinbami OS, Udoh SB, Idung AU. Self-medication: Potential risks and hazards among pregnant women in Uyo, Nigeria. Pan Afr Med J 2012;13:15.
17. Hakkarainen KM, Andersson Sundell K, Petzold M, Hägg S. Prevalence and perceived preventability of self-reported adverse drug events – A population-based survey of 7099 adults. PLoS One 2013;8:e73166.
18. Afolabi AO, Akinmoladun VI, Adebose IJ, Elekwachi G. Self-medication profile of dental patients in Ondo State, Nigeria. Niger J Med 2010;19:96-103.
19. Gimnig JE, MacArthur JR, M'bang'ombe M, Kramer MH, Chizani N, Stern RS, *et al.* Severe cutaneous reactions to sulfadoxine-pyrimethamine and trimethoprim-sulfamethoxazole in Blantyre District, Malawi. Am J Trop Med Hyg 2006;74:738-43.
20. Huovinen P. Resistance to trimethoprim-sulfamethoxazole. Clin Infect Dis 2001;32:1608-14.
21. Chinwendu O. The Fight Against Fake Drugs by NAFDAC in Nigeria. WHO; 2008. Available from: http://www.apps.who.int/medicinedocs/en/m/abstract/Js18405en/. [Last cited on 2014 May 03].
22. Quick JD, Boohene NA, Rankin J, Mbwasi RJ. Medicines supply in Africa. BMJ 2005;331:709-10.
23. Ognongo-Ibiaho AN, Atanda HL. Epidemiological study of fixed drug eruption in Pointe-Noire. Int J Dermatol 2012;51 Suppl 1:30-1, 33-5.
24. Babalola C. Drugs and mankind. In: Oguntomisin G, Edo V, editors. African Culture and Civilization – A Textbook for General Studies Programme (GSP). Nigeria: University of Ibadan; 2005. p. 136-52.
25. Oshikoya KA, Awobusuyi JO. Perceptions of doctors to adverse drug reaction reporting in a teaching hospital in Lagos, Nigeria. BMC Clin Pharmacol 2009;9:14.
26. Eland IA, Belton KJ, van Grootheest AC, Meiners AP, Rawlins MD, Stricker BH. Attitudinal survey of voluntary reporting of adverse drug reactions. Br J Clin Pharmacol 1999;48:623-7.
27. Okezie EO, Olufunmilayo F. Adverse drug reactions reporting by physicians in Ibadan, Nigeria. Pharmacoepidemiol Drug Saf 2008;17:517-22.