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Assessment of knowledge attitude and practice of pharmacovigilance by leaders in public health pharmaceutical supply chain in Nigeria.

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ABSTRACT

Pharmacovigilance involves the spontaneous reporting of adverse drug reactions (ADR) and ensuring the post-marketing surveillance of the quality and safety of medicines including phytomedicines and other pharmaceuticals used in the management of diseases. Its success depends on the awareness, attitude, and voluntary participation of healthcare personnel, patients, and institutions. This study aimed at examining the knowledge, attitudes, and practices of key pharmacovigilance actors in the public health pharmaceutical supply chain management in Nigeria. Consequently, a cross-sectional approach was used in the survey of 209 leaders of selected public health organizations. Purposive sampling technique was applied to administer validated semi-structured questionnaire electronically. Questions were drawn from the Nigerian national pharmacovigilance policy. Overall, response rate was 55%. Among the responders, medical doctors and medical laboratory scientists had better knowledge and practice of pharmacovigilance than pharmacists. Factors associated with practice of pharmacovigilance include awareness of policy (OR =1.90; P-value =0.1140), training provided by respondents' organizations (OR =1.34; P-value =0.4801), respondents' organization receiving periodic updates from the National Pharmacovigilance Center (OR =1.11; P-value =0.8525) and respondents independently receiving periodic updates (OR =0.83; P-value =0.7279). In conclusion, the study suggests pharmacovigilance outcomes could improve through increased awareness of the policy, training, and periodic safety communications.

Keywords: Pharmacovigilance, pharmaceuticals, supply chain, public health, practice.

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INTRODUCTION

Very recently, the race to mitigate the global fatality caused by the coronavirus disease 2019 (COVID-19) pandemic resulted in an unprecedented fast-track seen in the development and approval of vaccines with resultant modified clinical trial protocols [1]. This resulted in increased controversy including hesitancy surrounding the safety, efficacy, and the end-to-end supply chain integrity of the approved vaccines [2,3]. Equally, rapid progress was seen in the development of phytomedicinal prophylactics and immune boosting adjuncts for the management of COVID-19 [4]. Consequently, these happenings have re-emphasized the importance of a continuous (phase-VI) post marketing surveillance for all pharmaceuticals in the supply chain.

The risks associated with the use of medicines are well documented and medicines are known to cause unintended and avoidable harm including death [5]. Hence, medicines safety monitoring has remained important to the global healthcare community since the thalidomide tragedy of the 1960s [6]. For example, in Spain, at least 186 out of 4403 (4.2%) patients were urgently hospitalized within an observation period due to the untoward effects of drugs [7]. Similarly, in the United Kingdom, about 80% of ADR related incidents led to admission or prolonged hospitalization costing nearly £466m annually [8].

The unintended harmful effects of medicines are referred to as adverse drug reactions

(ADR). It is defined as “a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man” [9]. A related term is adverse event or experience which is defined as “any untoward medical occurrence that may present during treatment with a medicine, but which does not necessarily have a causal relationship with this treatment” [9].

The impact of ADR on consumers of medicines might include hospitalization, prolongation of hospital stays, visits to emergency departments, increased cost of care, congenital abnormalities, permanent disabilities, fatality, and others [10,11]. Similarly, hospital and healthcare systems bear increased cost burden associated with ADR management. Two main cost categories of concern are the cost of treating the ADRs and the cost of avoiding them [12]. Avoidance of ADR involves the cost associated with optimizing healthcare systems, overstretching available capacities, deploying individualized care; pharmacogenomics, regulating healthcare practices and products, setting up safety monitoring systems for medicines, and loss of confidence in the healthcare delivery system [13,14,15]. For example, in a resource limited setting like Nigeria, an estimated additional cost burden of 441.9 USD is incurred for a hospital management of ADR in a pediatric patient [16]. Also, in Canada, at least, 0.75% of total visits to the emergency department (ED) were ADR related in geriatric patients. At least, 21.6%

of the ED visits resulted in hospitalization attracting estimated ADR-related treatment cost burden of 333 USD for the ED visits and 7528 USD per hospitalization [17].

Historically, the development of organized medicines safety monitoring system started in response to the thalidomide disaster of the 1960s. The World Health Organization (WHO) coordinated global efforts in setting up an international medicines' safety monitoring [10,18,19]. This systematic approach is known as pharmacovigilance (PV).

Pharmacovigilance is defined as “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem” [9]. The WHO International Drug Monitoring Program was initiated in 1968 and coordinates spontaneous ADR reporting through National Pharmacovigilance Centers of member states, [20]. Spontaneous ADR reporting is defined as “a system whereby case reports of adverse drug events are voluntarily submitted by health professionals and pharmaceutical companies to the national pharmacovigilance center” [10]. This allows global knowledge sharing amongst NPC member states including some African countries who are recently becoming very active part of the WHO global system [21].

Pharmacovigilance is essential for a continuous post-marketing monitoring of

medicines after the carefully controlled phases of clinical trials [22,23]. In clinical trials, medicines are exposed to few (seldomly more than 5000) carefully selected candidates under controlled experimental conditions, [24]. Conversely, when medicines receive market authorization, particularly in cases of accelerated approvals as with the COVID-19 vaccines, they are exposed to a vast majority of uncontrolled heterogenous population impact [25].

Despite progress made in pharmacovigilance by developed countries and the international community, the situation is not the same in poorly resourced developing countries such as Nigeria [26,27]. The National Pharmacovigilance Centers in these settings have weak pharmacovigilance systems, poor data management framework, slow buy-in by the healthcare professionals as well as poor integration of the public and private-sector healthcare apparatus [28,29]. However, as with the developed countries, spontaneous reporting system for ADRs remains the mainstay and a cost-effective system for pharmacovigilance in resource-limited settings [30,31]. This method is affordable, scalable, and sustainable but its usefulness is limited by major challenges including awareness, attitude, and underreporting [32,33]. To proactively detect the harm associated with medicines and to have a representative spectrum of the harm within a population, through active participation of

all sectors of the healthcare system is recommended in the spontaneous ADR reporting activity [10].

Several knowledge, attitude and practice studies have been carried out globally and in Nigeria using qualitative designs to measure the awareness and involvement of stakeholders in pharmacovigilance in resource limited settings [34,35]. However, more work is required to evaluate the participation of the leadership of public health organizations involved in pharmaceutical supply chain management in Nigeria. Although some studies attempted an understanding of the public health organizations' involvement in pharmaceutical supply chain management in Nigeria, they however fell short of the needed inquest into the safety monitoring of the medicines in the supply chain [36,37]. This remains a challenge the Nigerian medicines regulator through the national pharmacovigilance policy holds pharmaceutical supply chain management organizations to account for the safety of medicines in the supply chain [38,39]. This study investigates how much pharmacovigilance is known and practiced in this sector given their involvement in mass distribution of pharmaceuticals including phytochemicals and vaccines.

METHODS

A cross-sectional approach was used to conduct a survey among leaders of public health organizations involved in the supply

chain management of pharmaceutical products including vaccines in Nigeria. Firstly, the questionnaire was designed using thematic pharmacovigilance focus areas drawn from the Nigerian national pharmacovigilance policy document. The questionnaire was then checked to be fit for purpose by experts in the Nigerian pharmacovigilance system. It was then field tested and adjusted for internal validation with a Cronbach's Alpha outcome of 74.3%. Online survey management system was used to administer the questionnaire based on email response collection channel.

Purposive sampling techniques was used to reach 209 public health leaders based on attendance registers of important national and regional meetings of public health pharmaceutical supply chain management organizations. Participation in the survey was voluntary following due informed consent. Reminder emails were scheduled to go out weekly for the four weeks' duration of the survey. At the end of the response collection, descriptive analysis of collated data was conducted using Microsoft Excel and SPSS version 25.0.

RESULTS AND DISCUSSION

Response rate was 55% (n =114) of which 59% (n =67) had adequate knowledge of pharmacovigilance (PV) and positive attitude. At least 33% (n =38) had adequate practice level. Key demographic categories of the responders are shown in Table-I below

while their responses are categorized in a matrix in figure-I.

Table I: Demographic categories of responders:

Respondent Type	Total	K	A	P	KAP
All	114	67 (56%)	67 (59%)	38 (33%)	26 (23%)
Postgraduate	96	58 (60%)	59 (61%)	33 (34%)	24 (25%)
Graduate	18	9 (50%)	8 (44%)	5 (28%)	2 (11%)
Govt (MoH)	29	18 (62%)	17 (59%)	13 (45%)	8 (28%)
Project Implementers	70	42 (60%)	42 (60%)	20 (29%)	15 (21%)
Donor Programs	30	7 (23%)	8 (27%)	5 (17%)	3 (10%)
Pharmacists	70	43 (61%)	43 (61%)	22 (31%)	16 (23%)
Doctors	4	3 (75%)	2 (50%)	2 (50%)	1 (25%)
Med. Lab. Scientist	10	7 (70%)	6 (60%)	4 (40%)	3 (30%)
Public Health	30	14 (47%)	16 (53%)	10 (33%)	6 (20%)

Where (K) represents knowledge, (A) represents attitude, (P) represents practice while (KAP) stands for knowledge, attitude, and practice.



Figure 1: Response matrix for knowledge attitude and practice

Our findings suggests that doctors and the medical laboratory scientists in the public health space have better knowledge of pharmacovigilance (75% and 70% respectively) than the pharmacists (61%). Also, doctors showed better practice than pharmacists (50% and 31% respectively). This may need to be further investigated as the relative number of responders of these professionals differed markedly. Overall, there was ~~only~~ 26% adequate knowledge/attitude/practice and 32% adequate knowledge/practice. This suggests a fair overall knowledge of pharmacovigilance but inadequate practice levels.

Further into the examination of factors that influence knowledge, attitude and practice of pharmacovigilance reveals more practice correlations that could serve as trigger points for continuous improvement interventions. The table of the comparative odds of the factors that influence the three attributes of pharmacovigilance, shows that awareness of the pharmacovigilance policy has great odds in all three attributes. Although, training in pharmacovigilance pursued independently by the individual shows the greatest odds (OR 2.93) relative to the attitude of the individual towards pharmacovigilance. However, this a favorable level of attitude may not necessarily translate into good practice.

Table 2: Comparative odds ratios for knowledge, attitude ad practice

Factors	Odds Ratios		
	K	A	P
PV training by individuals	1.32	2.93	0.95
PV training by institutions	1.74	1.74	1.34
Safety communication to individuals	0.65	0.65	0.83
Safety communication to institutions	0.43	0.43	1.11
PV policy awareness	2.32	2.32	1.90
PV policy accessible	1.93	1.93	0.82
ADR form accessible	0.88	0.88	0.90

Where (K) represents knowledge, (A) represents attitude, (P) represents practice

Furthermore, there was strong association between awareness of the pharmacovigilance policy and knowledge/attitude/practice (KAP) of pharmacovigilance, (OR =2.32; P-value =0.0301). This was the most significant factor the study suggests could promote knowledge and practice of pharmacovigilance. Hence, this thematic policy focus could be an important trigger to explore when planning a public health program for pharmacovigilance

intervention. In addition, periodic feedback communication by the National Pharmacovigilance Center to the supply chain management institutions also showed considerable association with knowledge (K) of pharmacovigilance, (OR =0.46; P-value =0.1579). Also, institutional training in PV provided by the public health programs had closer association with both knowledge (p-value: 0.1882) and knowledge/attitude/practice (p-value: 0.1025) respectively.

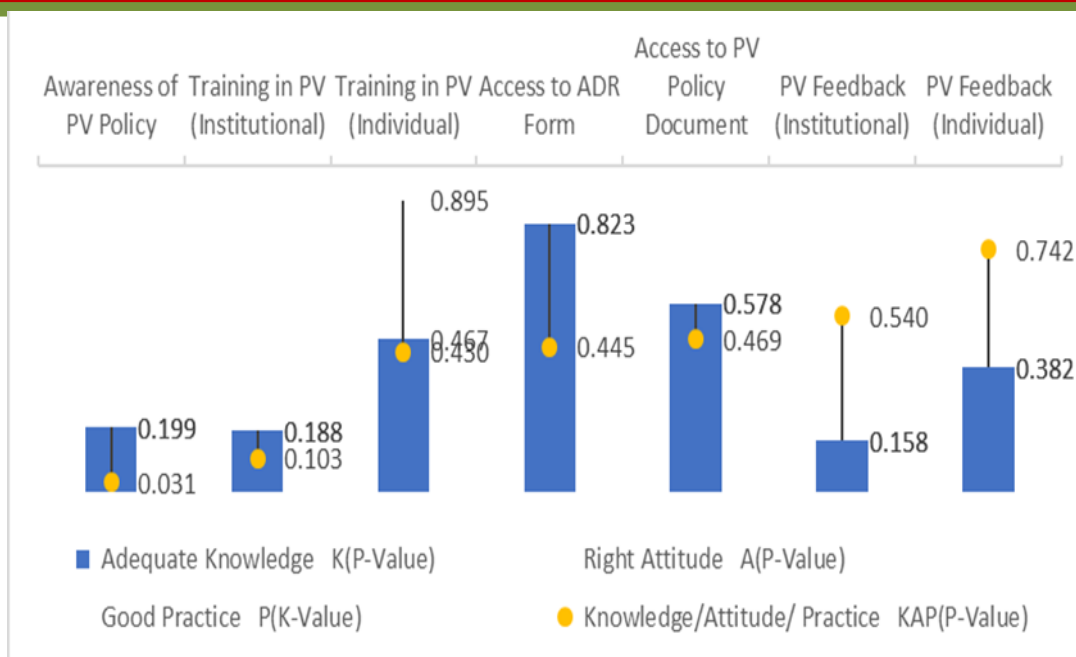


Figure 2: A comparison of the effects of factors affecting pharmacovigilance KAP on individuals and organizations

Limitations

Conducting an online data collection using email was a major limitation. It was difficult getting responses within the study time frame. Several reminders had to be sent with phone calls in some instances. This made the power of the study rather low. However, it did not affect the validity to the extent that this is a cross-sectional study.

Conclusion

In conclusion, the study suggests that pharmacovigilance knowledge, attitude, and practice of leaders in public health pharmaceutical supply chain management in Nigeria could improve through increase in awareness of the provisions of the national pharmacovigilance policy. Also, the effects

of periodic communication of medicines safety outcomes by the national pharmacovigilance center to the supply chain management organizations could equally enhance the knowledge attitude and practice of pharmacovigilance. In addition, training in pharmacovigilance provided to the leaders through their organizations could also show some effects. Overall, the study could provide insight into continuous improvement and systems strengthening for medicines safety practice and pharmacovigilance particularly among public health organizations involved in pharmaceutical supply chain management in Nigeria.

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