ejpmr, 2022,9(4), 07-19

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

KNOWLEDGE ATTITUDE AND PRACTICE OF PHARMACOVIGILANCE WITHIN HEALTH PROFESSIONALS, PHARMACEUTICAL COMPANIES AND DRUG REGULATORY ORGANIZATION IN CAMEROON

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Article Received on 24/01/2022 **Article Revised on 14/02/2022** **Article Accepted on 04/03/2022**

ABSTRACT

The drug discovery and development processes are designed to guarantee that medicines have the right quality, safety and efficacy. Unfortunately, the number of patients and volunteers who are exposed to drugs at approval gives only a small part of the story of adverse effects. It is therefore, mandatory in understanding the safety of medicines before and after approval by regulatory bodies. This post marketing surveillance can only be finally achieved after the drug is on the market through pharmacovigilance data. Health professionals, patients, drug manufacturers and drug regulatory authorities are therefore highly involved in the practice of pharmacovigilance (PHV). Cameroon imports 95 % of drugs and health care products. Therefore, an effective understanding of the knowledge, attitude and practice of Pharmacovigilance within the health sector by actors, would enhance the elaboration of the development of a good collaborative pharmacovigilance system platform in any country. This study has as objective to investigate the knowledge, attitude and practice of pharmacovigilance within health personnel, pharmaceutical companies and drug regulatory organs of the public health sector in Cameroon. A cross sectional, descriptive and analytical study was conducted in the Yaoundé Central Hospital (a Reference hospital), 50 pharmacies of the Mfoundi District and in 11 Pharmaceutical company representative offices in Yaoundé, and the Drug regulatory organ in Cameroon. The survey was conducted using a pre- tested self- administered questionnaire. A well-structured questionnaire for each study groups were. developed and used to pull data from the different study group. The data for health professionals and pharmaceutical companies was entered and analyzed using Epi-Info Version 3.5.4 statistical software and presented using Microsoft Excel spreadsheet. A total of 162 professionals composed of 11 (6.8%) Pharmaceutical companies representative office supervisors, 101(62.3%) Hospital personnel and 50(30.9%) Pharmacy personnel. These populations were subdivided into Hospital personnel comprising 8(4.9%) Specialists, 47(29%) General practitioners, 10(6.2%) Dentists, 30(18.5%) Nurses and 6(3.7%) midwives. Pharmacy personnel comprised of; 4(2.5%) Advanced level, 3(1.9%) HND (Higher National Diploma) or pharmacy technicians, 4(2.5%) bachelors holders and 39(24.1%) pharmacists. In the general appreciation of knowledge, 58% of pharmacy personnel, 52.9% of hospital personnel and 65.7% of pharmaceutical company representative supervisors had the right appreciation. For attitudes, 52% of pharmacy personnel, 43.4% of hospital personnel and 53.3% of pharmaceutical company representative supervisors had the expected results. For practice, 25.1% of pharmacy personnel, 17.5% of hospital personnel and 44.6% of pharmaceutical company representative supervisors had the right practice. This summed up to give a general appreciation of 33% for pharmacy personnel, 28% for hospital personnel and 39% for pharmaceutical companies, had a better appreciation of pharmacovigilance. Generally, there was little applicable knowledge which determined the poor attitudes developed towards pharmacovigilance among the health professionals and pharmaceutical companies leading to poor practice. Given that these are key actors in the pharmacovigilance system, these results are seen to cause the problem of underdevelopment in our Pharmacovigilance systems. This study calls for the need to scale up the technical platform and organization of a well-developed pharmacovigilance system in Cameroon.

KEYWORDS: Adverse drug reactions, Health Professional, Pharmacy personnel, Pharmaceutical company, Drug regulators, Yaoundé, Cameroon.

INTRODUCTION

The goal of pharmacovigilance (PHV) is to protect patients and the public wherever possible and to disseminate knowledge among the relevant professional communities and to patients in order to minimize risk.[1] This was coined following the tragedies which occurred

in the mid twentieth century. The thalidomide tragedy in the mid twentieth century triggered a chain of activities that were part of a global effort to avert a recurrence. Australia, Canada, several European countries, New Zealand and the United States of America established monitoring schemes based on reporting of suspected adverse drug reactions (ADRs).[2] From these beginnings emerged the practice and science of pharmacovigilance. Systems were developed in Member States for the collection of individual case histories of ADRs and evaluation of them.[3]

In 2007, national manufacturers held less than 5% market share on the amount of drugs produced by Cameroon.[3] This therefore means that Cameroon consumes more foreign supply of drugs, than locally manufactured drugs. These drugs manufactured by different Pharmaceutical companies are subjected to regulatory authorities external to Cameroon.

The need for pharmacovigilance is therefore paramount given that there is no legislation allowing the sampling of imported products for analysis in Cameroon.[4] Pharmacovigilance should not be perceived as a burden put upon the pharmaceutical product development industry by the regulating bodies. Once a drug is developed and approved, pharmacovigilance is essential to establish full safety data guaranteeing its survival in the market place.[5]

Cameroon who joined the WHO Program for International Drug Monitoring, known as the Uppsala Monitoring Centre (UMC) in 2010, is making some effort to get involved in pharmacovigilance.[1,3] In a bid to solve some of the problems caused by the inactivity in pharmacovigilance, the Minister of Health has been taking actions to quarantine drugs which have proven to have serious adverse reactions and withdraw from the market, drugs or batches of drugs with doubtable quality. An example occurred recently in January 2018 when Co-arinate tablets for Adults and children were quarantined for precautionary reasons, after a suspected serious adverse reaction was associated to administration of the drug.[5,6]

Pharmacovigilance is currently a public health issue in Cameroon, due to lack of good knowledge and practice of prescribers' physicians, pharmacists, nurses, and dentists who are not always aware of an existing pharmacovigilance system in Cameroon.[7-9] Given the quality of knowledge about our Pharmacovigilance system in Cameroon, the effective practice of pharmacovigilance can be encouraged by the pharmaceutical company representatives who are in charge of collection of data from patients and health care providers on the adverse effects of consumption of their products available on the Cameroon market. In view of the expected intervention of Pharmaceutical companies in acquiring Pharmacovigilance data, the need for sensitization, the procedures they follow and the rules they apply during acquisition of Pharmacovigilance information should be of great importance in this study.

Health care providers, patients and Pharmaceutical companies are therefore needed for the collection of data. It is important on Pharmaceutical companies to build up data for ADR of their new and existing molecules under repurposing, to guarantee quality, safety and efficacy of drug use.[8,9-11] This study aimed at building an understanding on the knowledge, attitude and practices of Pharmaceutical companies and public health actors in Pharmacovigilance.

METHODS

The study was a Cross sectional descriptive study, conducted in the Yaoundé Central Hospital., 50 Community Pharmacies in the Mfoundi District., 11 Pharmaceutical company representative offices and the drug regulatory Department of Pharmacy, Quality and safety for Drugs and Laboratories (DPML), in Cameroon. Hospitals were chosen following the Cameroon National Health System pyramid. Pharmacies that have been functional for at least 1 year were chosen from the list of pharmacies in the Mfoundi district. The Pharmaceutical companies were selected based on their consent and availability to respond to the questionnaires.

The timeline for the study was approximately 8 months, from October 2017 till May 2018. The target population was the health care professionals (medical doctors, nurses, midwives, pharmacists, dentists), pharmaceutical companies and the DPML. Included in this study were the health professionals having had at least 1-year work experience, Health professionals that were willing to participate in the study, and recognized pharmaceutical companies willing to participate in the study.

Sample size

The sample size was exhaustive of the population at hand, having estimated 60 pharmacists from the list of 112 pharmacies found on the pharmacy registered list in Yaoundé, 120 hospital personnel were approximated and 20 pharmaceutical companies. The National Pharmacovigilance centre for Cameroon and the Drug quality and safety laboratories (LANACOME). A cross sectional study with a structured questionnaire was used as a data collection tool for this study and was done with the acquisition of three data plans; The questionnaire for health professionals contained 15 questions, 6 to test knowledge, 5 to test the attitude, 3 to test practice.

Ethical consideration

Study was initiated after obtaining ethical clearance (Ref No/ 0957/UY1/FMSB/VDRC/CS of 25th May 2017, from the Institutional Ethics Committee (IEC of the faculty). The administrative authorizations were obtained from the directors of the structures involved in our study (the hospital, pharmacies and pharmaceutical companies selected for the study). Each health professional, pharmacist and representative of the pharmaceutical

companies participating in the study signed a written informed consent form before answering the questionnaire.

The study participants consisted of all the practicing healthcare professionals (medical doctors, specialist, dentists, nurses and midwives) who gave their informed consent and who are working at the hospital during the study period.

The questionnaire filled by Community pharmacy personnel contains 14 questions with 6 questions on knowledge, 5 questions on attitude and 3 questions on practice. The questionnaire for Pharmaceutical companies had a slightly different format presenting more questions on practice since they have a major role to play in processing the reports gotten and also in making available Adverse Drug Reaction report forms. The questionnaire contains 22 questions with 11 questions being based on Practice, 4 questions based on attitude, and 7 questions with knowledge as focus. The questionnaire for the DPML to be filled by the Pharmacovigilance Unit supervisor contains 3 knowledge questions, 3 attitude questions and 9 practice questions, since DPML had more information to give on practice of pharmacovigilance that any other aspect.

Collection procedure

From the contact with the health professionals, eligibility was sought. The objectives of the study and the modalities of participation were subsequently presented to the eligible professionals in order to obtain consent. Only those that freely consented were administered the questionnaire. The questionnaire was auto administered to prevent their answers from being influenced or pre meditated. Here, the participants completed the questionnaire themselves in the presence of the interviewer, who retrieved the filled questionnaire at the end of the exercise. Some, who were not available, answered and submitted on a second meet with the interviewer. The pharmaceutical companies were also administered questionnaires based on their consent. The questionnaires were retrieved once all the information required was made available. The DPML pharmacovigilance supervisor was interviewed after consent was given. The interview was done following the questions on the DPML questionnaire.

Data analysis.

The data collected was entered into a microcomputer using the Epi-Info version 3.5.4 statistical software for analysis. This was done following the three different populations of interest. Assembling the distinct data for each of them concerning the various variables of: Knowledge, Attitude and Practice. Considering the different groups, different roles and professions, they are all grouped separately, analyzing each variable in each population set which gave rise to results from which a conclusion was drawn. A positive response was considered as a correct answer and a negative or un attempted response was considered as an incorrect answer. Qualitative variables were expressed by percentages and the Chi-square test was used to compare the difference in correct responses for each question. Given the different professions and qualifications of the study population, two scoring methods were considered. As criteria for scoring, the model suggested by Essi *et al*.[6] in 2013 for KAP studies was used.

Criteria for scoring model

Table 1 illustrates the model for hospital personnel with the score and level of appreciation, ranging from less than 25% bad to more than 70% good

Table 1: Model for hospital personnel.

Score (Number of points)	Appreciation
Less than 25 %	Bad
Between 25 and 50 %	Insufficient
Between 50 et 70 %	Average
More than 70 %	Good

The model for community pharmacy personnel and pharmaceutical companies was different from that used for hospital personnel as seen in Table 2. This was as a result of the expected difference in exposure to pharmacovigilance principles.

Table 2: Model for community pharmacy Personnel and Pharmaceutical companies.

Score (Number of points)	Appreciation
Less than 50 %	Bad
Between 50 and 65 %	Insufficient
Between 65 et 85 %	Average
More than 85 %	Good

The results of health professionals and pharmaceutical companies were evaluated together as actors in pharmacovigilance, though they had completely different practice questions.

RESULTS AND DISCUSSION

Sociodemographic profile.

Of A total of 190 people given questionnaires, 162 questionnaires were properly filled and thus could be exploited which made up a percentage of 85.3 % questionnaires exploited. Of the 162 participants, there were 50(30.9 %) pharmacy personnel, 101(62.3 %) hospital personnel and 11(6.8 %) PCRSs were obtain. When analyzing the possible associated factors which could influence Pharmacovigilance practice, these sociodemographic factors were considered. Significant p-values considered were values lower than 0.05 gotten through the Chi-square test.

Qualification had an influence on pharmacovigilance knowledge and gave significant p-values of 0.010 in pharmacists, 0.010 in specialists, 0.000 in general practitioners and 0.000 in nurses. The influence of qualification on pharmacovigilance attitudes gave a

significant p-value of 0.010 in specialists and 0.040 in dentists.

Qualification of the personnel involved

In the pharmacy sector 78% had PharmD, while at the hospital 47% where degree holders followed by 30 % Nurses with Diplomas. In the pharmaceutical companies most of the staff had above advance level. The summary of qualification of study population has been described in table 3.

Table 3: Population and Qualification.

	Pharmacy		**Hospital**		**PCRSs**		**All**
Population	50(30.9 %)		101(62.3 %)		11(6.8 %)		162
Qualification / Profession	Advanced level	4(8 %)	Mid wife	6(5.9 %)	Supervisor	11(100 %)	
	Pharm tech	3(6 %)	Nurse	30(29.7 %)			
	Bachelors	4(8 %)	Dentist	10(9.9 %)			
	Pharm D	39(78 %)	G.P	47(46.5 %)			
			Specialist	8(7.9 %)			

Work experience

The work experience registered for the health personnel is elaborated in table 4, where nurses and midwives showed the greatest number of years of experience. The influence of work experience on pharmacovigilance knowledge gave a significant p-value of 0.010 where work experience was <5 years among pharmacy personnel and 0.040 where work experience was between 10 to 14 years among hospital personnel.

Table 4: Work experience of the population.

	Work experience	**<5years**	**5-10 years**	**11-15 years**	**16-20 years**	**>20 years**	**All**
	Pharmacist	35	1	2		1	39
Pharmacy	Bachelors	2	1	1			4
	Pharmacy tech	2	1				3
	A/L	1	2	1			4
	Total	40	5	4		1	50
Hospital	Specialist	1	7				8
	G. P	44	3				47
	Dentist	8				2	10
	Nurse	8	10	6	1	5	30
	Midwife	1	2	1		2	6
	Total	62	22	7	1	9	101
Pharm company	Supervisor	3	1	5	1		11

An appreciation of study area

The health professionals were questioned on where they got their training. The idea was based on a presentation of either in country (local) or out of the country (foreign).

Site of study influenced pharmacovigilance attitudes gave a significant p-value of 0.030 when pharmacy personnel studied locally, 0.030 when pharmacy personnel studied in another country, 0.030 when hospital personnel studied in another country, and 0.030 when they studied locally.

Pharmacovigilance practice was influenced by site of study giving a significant p-value of 0.030 where the pharmacy personnel studied in another country. Figure 1 is an illustration of the study area of the health professionals.

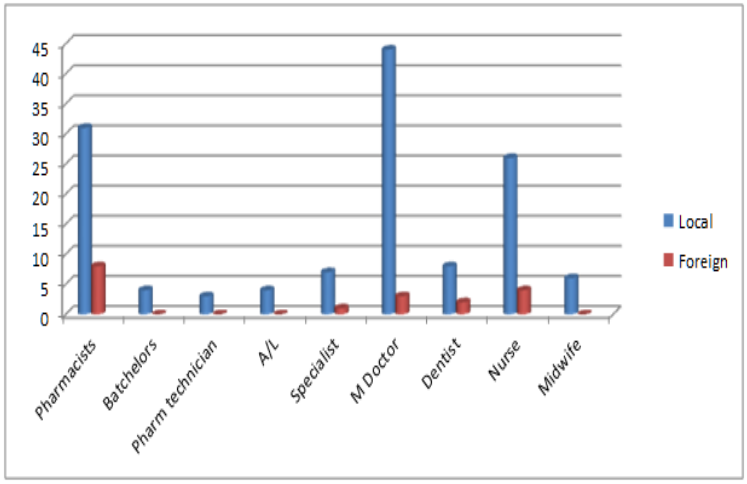

Figure 1: Study area of Hospital and Pharmacy personnel.

Results for pharmaceutical companies representative office supervisors

Sociodemographic factors

Out of 15 companies who received the questionnaire, 11 Pharmaceutical successfully responded to the questionnaire. Of the 11, 10 of them have been existing in Cameroon for more than 10 years. The table 5 gives an appreciation of the duration of existence in Cameroon and the number of companies in each range.

Table 5: Company time of existence in Cameroon.

Company Existence in Cameroon		N %
<10	1	9.10
10-19	9	81.8
20<	1	9.10
Total	11	100.

Knowledge of pharmaceutical companies

The figure 2 indicates appreciated level of knowledge of hospital personnel. 27.3% of the population that is 3 people was estimated to have an insufficient knowledge of Pharmacovigilance. 3 supervisors therefore presented poor knowledge. 7 people or 63.6 % of the population had average knowledge. 1 person, giving 9.1 % of the population had a good score.

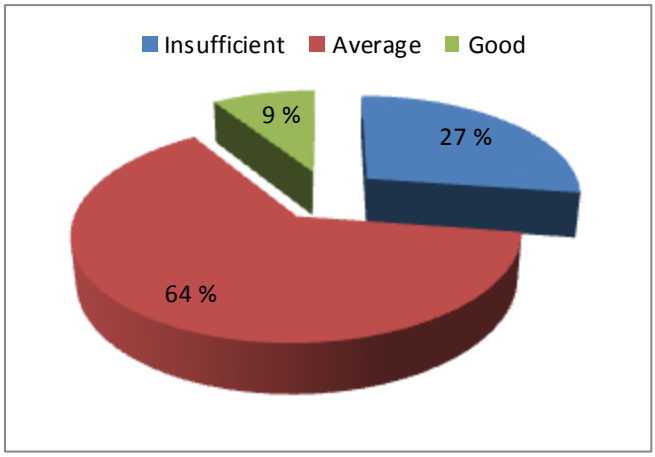

Figure 2: Knowledge of pharmaceutical companies.

Attitudes of pharmaceutical companies

The chart above is a demonstration of the attitude of the population to Pharmacovigilance. This was seen to consist of 5 people (45.45 %) having a harmful or bad attitude, and 5 people (45.45 %) with an erroneous attitude. These two scores summed up gives 10 people or 90.9 % of the population presenting poor pharmacovigilance attitudes.

Only 1 person or 9.10 % of the population was seen to have a good pharmacovigilance attitude.

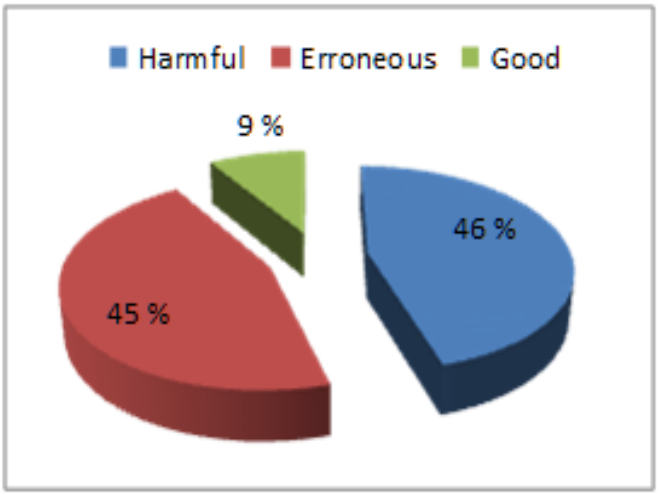

Figure 3: Attitude of pharmaceutical companies.

Qualitative results for department of pharmacy, Drugs and Laboratories (DPML)

Sociodemographic profile

The respondent was the Supervisor of the Pharmacovigilance unit in the DPML.

He had been in service at this post of responsibility for 3 years.

Knowledge

The medical doctors, pharmacists and nurses were involved in Pharmacovigilance reporting in recent years. Pharmacovigilance was focused on providing information about adverse effects experienced after administration of particular drugs. Medical personnel are supposed to have a constant supply of Adverse Drug Reaction forms. Pharmaceutical sales representatives and Representative from the Ministry of Health were all supposed to be involved in supplying ADR forms but were not compelled to by legislation.

Attitudes

Unexpected Adverse Events are the kind of Adverse events pharmaceutical companies have notified regulatory authorities about recently. Pharmaceutical companies were not obliged to sensitize medical personnel about Pharmacovigilance reporting because there was no law compelling them to do so. The DPML did not have sufficient control over the activities carried out by Pharmaceutical companies in Cameroon due to lack of enforcement or lack of application of the pharmacovigilance regulation in place.

Practice

There was no published legislation for pharmacovigilance in Cameroon. There were no Pharmacovigilance representatives in Reference Hospitals in Yaoundé, but there were pharmacovigilance representatives spread out through the regions in Cameroon. During homologation of a pharmaceutical company there is no agreement made to receive reports of all adverse drug events. The DPML did not always receive Periodic Safety Update Reports from pharmaceutical companies active in Cameroon. The DPML did not always give feedback to these reports as they are not regular.

Pharmaceutical companies rarely sent notifications in cases of ADRs. There was no set time frame of submission from when the case is documented since there were no established pharmacovigilance legislation in Cameroon. The DPML has taken steps severally to minimize adverse effects reported by Pharmaceutical companies and health personnel. It was not yet mandatory for each pharmaceutical company to have a Qualified Personnel for Pharmacovigilance due to absence of pharmacovigilance legislation. In the absence of Pharmacovigilance legislation, the regulation of which ADR form is to be used during documentation of ADRs is not spelled out.

Therefore, both the pharmaceutical company's ADR form and the Ministry of Public Health's ADR form could be used. The study focused on the appreciation of Pharmacovigilance by Pharmaceutical companies, in the Mfoundi district.

Public health actors

In a bid to appreciate this behavior, a questionnaire comprising questions on knowledge, attitudes and practices was auto administered to public health actors who concerted to participate. The questionnaire was given to 190 people and was responded properly by 162(85.3 %) people. Precisely 11 (6.8 %) Pharmaceutical company representative office supervisors (PCRSs), These populations were subdivided according to various qualifications. According to the appreciation of Fokunang *et al*.[5] in 2017 in Cameroon, the required

distribution proportions of personnel in hospitals was taken into consideration in this study but not at the same percentages.

It was seen that 80 % (n=40) of the pharmacy population had less than 5 years of work experience. The left over 20 % (n=10) were split in two, with 10 % falling within the range of 5- 10 years' work experience, 8 % falling within the range 11- 15 and 2 % having over 20 years work experience.

Hospital personnel had 61.4 % (n=62) with less than 5 years of work experience, 21.8 % (n=22) falling within the range of 5- 10 years' work experience, 6.9 % (n=7) of the population falling within 11- 15 years of experience. 8.9 % (n=9) had over 20 years of experience and only 1 person had experience between 16-20 years.

Pharmaceutical companies' supervisors on the other hand had their highest population of 45.5 % (n=5) with 11-15 years' work experience, 27.3 % (n=3) had less than 5 years' work experience and 9.1 % fell within the 5-10-year range and the 16-20-year range. The number of years in service was seen to affect the pharmacovigilance behavior particularly in the aspect of knowledge as seen in Toklou and Uysal[12,13,18] in 2008 in Turkey where Pharmacy personnel had a significant p-value of 0.01 for those with less than 5 years of work experience.

Pharmacovigilance reporting.

With regard to pharmacovigilance reporting, this study is one of the first to assess the knowledge, attitudes and practices of Cameroonian health professionals and Pharmaceutical company representative office supervisors (PCRSs). In appreciating the knowledge level of Pharmacy personnel, Hospital personnel and PCRSs, the definition of Pharmacovigilance was considered. The majority of people could define pharmacovigilance, precisely 77 % of Hospital personnel, 82 % of pharmacy personnel and 90% of PCRSs. The study conducted by Toklou and Uysal[18] in 2008 in Turkey had contrary results with the minority being able to answer positively. The difference in responses can be attributed to the fact that they had open questions for pharmacists to reason out for themselves, thus raising difficulty. Our case served as a reminder to most of the professionals. The Uppsala Monitoring Centre as well as the Ethiopian Pharmacovigilance center justifies the intervention of general practitioners and specialists, pharmacists, dentists, midwives, nurses, manufacturing companies and patients in pharmacovigilance reporting.[14,15,16] In our study 61.1 % Hospital personnel, 61.3 % of Pharmacy personnel and 69.7% PCRSs had the right appreciation of the actors involved. According to Fokunang *et al.*[5] in 2014, 44.7 % of their population knew these actors. This has improved to 64 % in the present case. The DPML presented 3 actors as having participated in Cameroon in recent years. These were medical doctors, pharmacists and nurses. The objective of pharmacovigilance as seen in the study conducted by Wysowski and Swartz.[19-22] in 2005 was clear to the majority of personnel with a general appreciation of 91.4 %.

Less than half of the general population (29.6 %) was able to identify all the adverse events expected to be reported. Results from Fadare *et al.*[22,24] in Nigeria in 2011 show that; a majority (>70 %) of the respondents were aware of the adverse events to report. This was much higher than our case, probably because as seen in Uppsala records,[6,25] Nigeria who got implicated in reporting since 2004 is more mature than Cameroon who got involved only in 2010.

About three quarters of the population (76.5 %) knew we have a drug regulatory authority in Cameroon, but only 35.2 % knew its name. In a study conducted by Srinivasan *et al.*[26,27] in India in 2017, 59.5 % of their population knew their regulatory authority. The difference in level of activity of these authorities within the different countries defends these results. Of this record, almost all PCRSs (90.9 %) knew this since they have a greater exposure to the DPML, not only as a pharmacovigilance regulatory office, but also as the Marketing Authorization provider.

Need for constant availability of pharmacovigilance form

The PCRSs were questioned on the need for a constant supply of pharmacovigilance forms to medical professionals. All of them acknowledged the need. 10 out of 11 of them indicated that pharmaceutical sales representatives are supposed to lead in supplying health professionals with these forms and only 2 of them suggested ministry of health representatives could take charge. This could prompt an assumption that the pharmaceutical companies constantly supply pharmacovigilance forms to health professionals. The DPML declared both the pharmaceutical sales representatives and the ministry of health representatives are expected to make available the pharmacovigilance forms.

Knowlegde PCRs

As a general appreciation of knowledge, the PCRSs had 37 % of good responses as compared to 33 % in pharmacy personnel and 30 % in hospital personnel. They therefore had a better mastery of pharmacovigilance than pharmacy personnel and hospital personnel whose knowledge was seen to be the least among them all. This can be accounted for by the general difference in manipulation and expected mastery of drugs and pharmacovigilance by pharmaceutical companies and pharmacists.

PCRSs had the best knowledge with only 27 % having poor knowledge. They had 27 % of the responders with insufficient knowledge, 64 % with average knowledge but only 9 % had good knowledge. These results showed

the Pharmaceutical companies were not ignorant of pharmacovigilance and the role they should play. The results would also greatly improve when implementation is increased. From the above results we can see the need for more pharmacovigilance awareness in our society. As described by Toklou and Uysal[18,28] knowledge and attitudes exert a strong influence on pharmacovigilance reporting We assume that if the modalities surrounding pharmacovigilance reporting are clearly stated to the health professionals there would be better knowledge of the practice and consequently better reporting.

Need for pharmacovigilance reporting

The necessity of pharmacovigilance reporting was seen by almost every respondent with a percentage total of 97.4 %. This was similar to the results of Palaian *et al.*[29,34] in 2011 in Nepal and Gupta et al[30,31,46]l in South India who found 96.6 % and 97 % response respectively.

Expected reaction of health professionals to PHV

In this study, the question on the expected reaction of health professionals had very low response level of 38 %. Hospital personnel made up only 31.9 %, pharmacy personnel made 39% and PCRSs who were suggesting what should be done, made only 43.2 %. The majority of health professionals selected 'stop administration' which was the first basic thing they do when faced with an adverse event. The next considered proposition was 'change of treatment therapy' where 35.6 % of hospital personnel and 28 % of the pharmacy personnel participated.

The PCRSs suggest all health professionals fill and submit pharmacovigilance forms meanwhile only 24 health professionals acknowledged their participation. The last proposition to 'inform drug representatives' was least solicited. The WHO drug monitoring center states that drug monitoring is also done by pharmaceutical companies[32,33] thus the need for informing and filling an pharmacovigilance form. These results prove the absence of the pharmacovigilance reporting habit in our society because the health professionals and the PCRSs lack valid information concerning pharmacovigilance reporting and the management of ADRs as a whole.

Availability of pharmacovigilance form PCRSs

The availability of the pharmacovigilance forms was also questioned. 54.5 % of the PCRSs supported the idea that the forms were to be made available after being requested. 45.5 % were for the idea that the forms needed to be supplied constantly or without a specific request. These responses could be seen as the center of the pharmacovigilance sensitization problem since, if the health professionals are constantly supplied with pharmacovigilance forms, the interest to know what to do with them will be raised. The forms could then be used as a first step to the sensitization of pharmacovigilance.

Comparing general attitude of the study population

In comparing the general attitudes of the three populations, the PCRSs presented the best attitudes of 53.3 %, and could be considered as having an average attitude. The pharmacy personnel followed with 52 % and hospital personnel with 43.4 %. This can be compared to Gupta et al[35,37,46] in 2015, in India, who had an average attitude response of 82.2 % contrary to our case of 46.8 %. This can be as a result of their greater exposure due to active presence of pharmaceutical companies in their society and the establishment of adequate legislation handled by the Pharmacovigilance Program of India (PvPI)[32,35] guiding these companies in their function.

Attitude scores

Attitude scores bring out the Pharmacy personnel having the best attitudes with only 48 % having poor attitudes in pharmacovigilance. They had 8 % with harmful attitudes, 40 % erroneous, 34 % average and just 18 % good attitudes. These are poor results but comparatively better than the other populations. Hospital personnel had a poor attitude score of 69 % which was considerably higher than pharmacy personnel. The details include 4 % being harmful, 65 % having erroneous attitudes, 23.8 % presenting average attitudes and only 6.9 % had good attitudes in pharmacovigilance. They were also much less exposed to pharmacovigilance and thus, this could be expected.

The PCRSs had the lowest attitude score. They had about 91 % poor attitude which reflects their low impact in Cameroon, contrary to what they are supposed to present.

The results above can draw us to think pharmacovigilance has not been properly introduced in Cameroon, as the actors of pharmacovigilance have a general poor attitude. The health personnel need to develop the right attitudes, getting familiar with pharmacovigilance reporting and the forms used. The Pharmacovigilance practice, after having had an idea of the knowledge and attitudes of hospital personnel, pharmacy personnel and PCRSs, becomes of great interest.

The hospital personnel and pharmacy personnel who have participated in pharmacovigilance make up just 20(13 %) people out of the total 151 health professionals in the study with 13 pharmacy personnel and just 7 hospital personnel. In similar studies conducted by Srinivasan *et al.*[26,37,38] in 2017, and Palaian *et al.*[34] in 2011, they had 36.5 % and 33.7 % respectively of their populations who had participated in Pharmacovigilance reporting. These were also below average but they could still be considered as double our present state. This therefore proves the level of underreporting in Cameroon is much higher than that in India and Nepal

Sources of pharmacovigilance forms in cameroon.
Following the majority of respondents (n=11), the forms made available for the few cases above were Pharmaceutical company forms. The forms were supplied by the pharmaceutical sales representatives. The ministry of public health forms were used by 9 respondents being downloaded from the internet for 3 of the respondents and supplied by ministry of public health representatives for the other 6 respondents. In a study conducted by Toklou and Uysal[18,43] in 2008, the health professionals acknowledged that difficulty in accessing forms is a great factor for underreporting. This is acknowledged in our case since those without access to forms do not end up reporting.

Outcome of submitted pharmacovigilance forms
The health professionals expect to receive certain responses after submitting pharmacovigilance reports. 73 % expect to receive instructions from the DPML, 59 % expect to receive information about the drug in question, only 32 % thought receiving a safety alert was important. 24 % of these professionals considered the withdrawal of the product and only 21 % thought modification of the leaflet is a worthy response. Only 29.3 % of the population thought all the propositions were worth expecting. From the WHO guidelines,[44,46] pharmacovigilance reporting is encouraged when a reporter receives feedback from the authorities. This highlights the problem of health professionals not being well informed about pharmacovigilance reporting.

Less than half of the health professionals (41.7 %) were of the opinion that the pharmaceutical sales representatives sensitize them on pharmacovigilance as declared by most of the pharmaceutical companies. This result adds more justification to the idea that the pharmaceutical companies are not fully playing their role in the pharmacovigilance system.

The PCRSs having different questions from health professionals were appreciated accordingly.

The majority of the PCRSs (72.7 %) felt they were obliged to notify pharmacovigilance cases to the authorities but only 63.6 % acknowledged they actually report. The DPML on the other hand made it clear that in the absence of legislation, the pharmaceutical companies are not obliged to report, although some report out of their free will. The Uppsala guidelines,[6,42] lay emphasis on the on the importance of this reporting and general communication between these two bodies.

PCRSs were asked how a pharmacovigilance form was treated after it has been filled. 72.2 % said it was first analyzed by the company, 27.3 % were of the opinion that the company analyzed and sends feedback to the reporter. Only 9.1 % shared the opinion that the countries forms be transmitted to their pharmacovigilance authority. None of the supervisors shared the opinion of storing the report in the company's database. The European Medicines Agency in their Guidelines for good pharmacovigilance practice stipulated that the listed steps all intervene in the processing of pharmacovigilance data.[23,35] Due to underreporting, the expected reflex responses which come from frequent exposure to pharmacovigilance practice are not seen. Out of 11 Pharmaceutical companies involved in the study, only 4(36.4 %) had ADEs in their databases. Out of the 4, only 1 of the companies had 20 ADE cases recorded, another had 3 cases and 2 of them had just 1 case recorded each. This was a clear manifestation of the poor pharmacovigilance practice influenced by all the pharmacovigilance actors discussed in our study.

Minimization methods were considered only by 2 pharmaceutical companies out of 11. This number was this low because the pharmaceutical companies had no obligation on pharmacovigilance regulations in Cameroon. They were therefore not urged to sensitize for reports to come in, analyze and develop information and finally consider a minimization method. The DPML on the other hand takes measures whenever necessary to minimize ADRs, even though most of the cases do not come in through Pharmaceutical Company reports or notifications. A most recent example can be seen in the withdrawal of Cotrimoxazole 240mg/5ml pediatric oral suspension in May 2018 in Cameroon.[27,30]

All pharmaceutical companies had a qualified person for pharmacovigilance (QPPV). 10 of them mentioned the existence of established pharmacovigilance departments and only 2 PCRSs, confirmed the existence of a PV unit in Cameroon. The DPML confirmed this, acknowledging that in the absence of pharmacovigilance legislation, the pharmaceutical companies cannot be forced to have a qualified person for pharmacovigilance in Cameroon. The availability of the QPPV is one of the major components of a well-established PV system as seen in the pharmacovigilance and risk management chapter of Global Clinical Trials.[12]

All pharmaceutical companies facilitate or stimulate pharmacovigilance reporting by provision of pharmacovigilance forms when demanded. Only 2 pharmaceutical companies mentioned sensitization of medical personnel on the use of pharmacovigilance forms. Just 1 pharmaceutical company trains its personnel on PV reporting procedures. Only 1 pharmaceutical company trains its personnel on the expected ADRs of their products. None of the pharmaceutical companies deposit pharmacovigilance forms at health care facilities. This is contrary to what the Uppsala guidelines where pharmacovigilance reporting is facilitated when there is easy access to report forms.[24,44] This implies most of the necessary actions which could promote pharmacovigilance reporting have not been effected, thus our high level of underreporting.

All the PCRSs indicated that pharmaceutical sales representatives are trained on the pharmacology of the

drugs they represent but only 1 pharmaceutical company out of 11 trains its sales representative on pharmacovigilance procedures. These two elements which are supposed to be taught together are separated, with the pharmacovigilance training seeming less important. Since effective distribution and sensitization of health professionals about Pharmacovigilance report forms can only be done by a sales representative who has been trained in that domain.

To compare the general practices of the three populations, the PCRSs present the best practice of 44.6 % which is below average but better than pharmacy personnel with 25.1 % and Hospital personnel with 17.5 %. This proves that pharmacovigilance practice in Cameroon is far below average. The average practice rate is 29.1 % which is far lower than 55.5% found by Palaian *et al.*[34,41] in 2011 in Nepal. Given that Nepal joined the WHO Program for International Drug Monitoring in 2006, while Cameroon joined in 2010,[13] we suggest that over the years its advancement in instituting pharmacovigilance be much higher and more stable than Cameroon.

Practice scores are very low and suggest that the Pharmaceutical companies, having the best practice with only 9.1 % having average practice and 90.9 % with poor pharmacovigilance practice. Hospital personnel had a poor practice score of 99 % which is considerably higher than pharmacy personnel who had 100 % poor practice. The details for hospital personnel had 87 % being bad, 12 % inadequate practice and only 1 % presenting average practice. The pharmacy personnel had 98 % with bad practice, and 2 % with inadequate practice. These scores demonstrate the problem of underreporting we experience.

The pharmaceutical companies having an upper hand over the health professionals have a better score but need to get more involved in pharmacovigilance sensitization for there to be an evident increase in practice levels.

In a bid to evaluate the general scores of each of the study populations, the pharmacovigilance skills developed were evaluated. The hospital and pharmacy personnel had better skills in pharmacovigilance, with hospital personnel having a higher quality since they had 14 % good skills and 17 % acceptable skills compared to 10 % good skills and 21 % in pharmacy personnel. The pharmaceutical companies had only 6 % good skills and 24 % acceptable skills. These skills are all far below average, reflecting the results from the knowledge attitude and practice which were all generally much lower than other countries who did studies on health professionals like Nigeria, Nepal, India, Turkey.[18,26,44] The uniqueness of this study makes comparison with other studies give us a rough appreciation and not a vivid image of the situation.

The General appreciation of all the populations studied; hold a very low practice rate of 33.3 %. Pharmaceutical companies, pharmacy personnel and the hospital personnel all need to emphasize on gaining adequate knowledge required to develop the right attitudes leading to the desired practice in pharmacovigilance. If this is done the pharmacovigilance system in Cameroon will experience a face lift. Gupta *et al.*[46] in 2015 emphasized on the necessity for each country to assess the knowledge, attitude and practice of its pharmacovigilance actors, across different healthcare facilities, at regular periods so as to monitor the evolution and progress made as well as see the faults to better plan ahead. If the required changes are applied, there will be a marked difference between the results of upcoming studies and the present one.

Some of the difficulties faced in this study in Yaoundé, were first to do with coordinating the three structure, two of which were health structures having personnel of different trainings and educational levels, hence causing a difference in perception. To address this problem, evaluation and scoring had to be done differently taking into account the appreciated difference in training and exposure to the topic. We had limitations regarding sample size as this study was conducted in only one hospital as a pivotal study to give a rough appreciation of health professionals in other hospitals and hence difficult to extrapolate the study findings to the entire country. Some Pharmaceutical company representative offices did not have very clear pharmacovigilance practices, which made them less enthusiastic about participating or responding to our questionnaires. The objective was achieved however to provide and insight through the investigation of the knowledge, attitude and in some pharmaceutical companies and among the public health actors, assessing the practice and procedures put in place for documentation of adverse drug reactions among health personnel, pharmacy staff, pharmaceutical company representatives and our drug regulatory authority.

CONCLUSION

The following conclusions could be drawn from the study:

The pharmacovigilance knowledge for the hospital personnel, pharmacy personnel and pharmaceutical companies in our Country were above average but could not be rated as good in Pharmacovigilance. The pharmaceutical companies have a percentage of 65.7 % in pharmacovigilance knowledge which was higher than the others but still below average. This knowledge, if improved would have a better manifestation in the general behaviours of health personnel towards pharmacovigilance.

The pharmacovigilance attitude observed in the study was generally below average, with pharmaceutical companies still showing the highest attitude an upper hand with just 53.3 %. Attitudes which develop after

knowledge has been gained, could not give better results than this seeing the level of knowledge the population had.

Pharmacovigilance practice yielded results far below average for all the populations studied. Pharmaceutical companies still took the lead in pharmacovigilance practice but with 44.6 % which was clearly below average. This could be accounted for by the lack of legislation which could motivate pharmaceutical companies to do their part in improving the situation. The hospital personnel and pharmacy personnel had very low rates of 17.5 % and 25.1 %. These results manifest the underdevelopment in our pharmacovigilance system.

The study therefore justified the hypothesis since little knowledge, gave rise to less attitudes and consequentially much less practice. There was a great need for the pharmacovigilance system in Cameroon to develop through sensitization.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

EATF, CNF, MJE conceived the study and designed the methods. BH, TMVE, and NBN did the experimental and laboratory work, collected data and other materials. EATF, LBF, NBN drafted the manuscript. TEAF, MJE, NA, TYO, and FCN edited and finalized the manuscript for publication. All authors read and approved the final manuscript.

ACKNOWLEDGEMENTS

This project was partly privately funded and contribution from the Research Mobilization support funds from the Ministry of Higher Education of the Republic of Cameroon. We greatly acknowledge the technical support of the laboratory for preclinical animal and pharmaco-toxicology research of the Faculty of Medicine, The University of Yaoundé 1, Cameroon

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