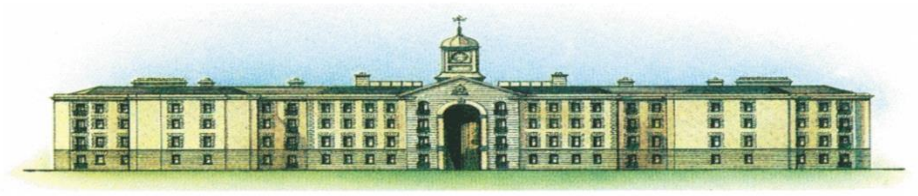

Griffith College

An Analysis on the Assessment and Reporting of Adverse Drug Reactions in Tertiary Hospitals in Lagos State, South-West Nigeria".

Research dissertation presented in partial fulfilment of the requirements for the degree of MSc in Pharmaceutical Business and Technology (QQI)

Innopharma/Griffith College Faculty of Pharmaceutical Science

Dissertation supervisor: Dr. Prosper Anaedu

Zainab Abolanle Atobatele

August 2020

CANDIDATE DECLARATION:

Candidate Name: Zainab Abolanle Atobatele

I certify that this dissertation titled:

“An Analysis on the Assessment and Reporting of Pharmacovigilance (Adverse Drug Reactions) In Tertiary Hospitals in Lagos State, South-West Nigeria” submitted for MSc in Pharmaceutical Business and Technology is the result of my own work and that where reference is made to work of others, due acknowledgment is given.

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Date: 28-August-2019

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Date: 28-August-2020

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ABSTRACT

Due to repeated occurrence of serious, unexpected ADR over the years, lots of professionals and public attention has been drawn to ADRs, and this has led to more focused attention on drug safety surveillance system. ADR incidence is associated with high rate of morbidity and mortality and this incidence cut across all age groups with a large number of hospitalisation, and huge financial burden on Nigeria healthcare system and the society. Unfortunately, the assessment, monitoring, and reporting system of ADR in Nigeria healthcare system still have lots of room for improvements, especially with the involvement of tertiary hospitals in Nigeria. Due to the above-stated problems, the assessment and analysis of ADR are critical to promptly detect the likely safety and security issues that might be associated with medicinal products; hence this research aims to analyse assessment and reporting of ADR in Tertiary Hospitals in Lagos State, South-West Nigeria".

The purpose of this research is to identify bottlenecks and loopholes in the system that hinders effective ADR practice in tertiary hospitals in Lagos state Nigeria. The research involved major stakeholder of pharmacovigilance activities which includes; HCPs (Doctors, Nurses, and pharmacists) and patients of tertiary hospitals. It aims to interact with HCPs to determine their perception towards direct patient reporting of ADR. Also patients were considered in the study to determine their level of awareness/knowledge towards ADR reporting.

The primary data was collected using an online survey and phone interview. The survey was targeted at 450 participants, and a total of 405 respondents were obtained in return in which 270 were patients, and 135 were HCPs (doctors, nurses, and pharmacists) recording a response rate of 90%. For the interview, 12 people were scheduled to be interviewed but 6 responses were obtained in which 2 were doctors, 2 were nurses, and 2 were pharmacist recording a response rate of (50%).

From the analysis conducted a significant number of the HCPs participants have basic understanding of ADR but have no knowledge of causality assessment and they established that they are not sufficiently trained on how to assess and report ADR. Several bottlenecks such as lack of knowledge/awareness, lack of feedback from NPC, unavailability of ADR reporting forms, insufficient staffs, cumbersome procedures, and excessive workload were established as most challenging issues. However, a highly significant number 92% are willing to update their knowledge on ADR practice and opted to make it a mandatory obligation to help resolve underreporting issues faced by the country.

A significant number of Patients participants established they are not familiar with ADR and the importance of reporting, while the HCPs also acknowledge that they are not aware that patients can report ADR directly neither do they think it is a good idea because they are of the perception that patients can't generate a valid/quality ADR reports.

Creating more awareness for both HCPs and general public, organising frequent training, workshop and seminars to update the knowledge of HCPs, providing adequate resources, incorporating ADR module into the curriculum of HCPs both during their undergraduate and orientation program when newly employed, establishing an active pharmacovigilance centres in tertiary hospitals to help monitor and guide ADR practice, educating and encouraging patients on ADR reporting and it is importance, are sustainable recommendations that will improve ADR practice and contribute invariable to pharmacovigilance system in Nigeria.

Key Words: Pharmacovigilance, Adverse Drug Reactions (ADRs): awareness, knowledge, challenges, causality assessment, ADR assessment and reporting, Direct patient reporting, Healthcare Professionals (HCPs), Nigerian Agency for Food and Drug Administration and Control (NAFDAC), National Pharmacovigilance Centre (NPC), SMS code, ADR forms/yellow card scheme, and e-reporting forms.

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CHAPTER 1: INTRODUCTION

1.1 Overview of the Study

Medicinal products are expected to save lives and maintain public health as "dying from a disease is sometimes unavoidable; dying from medicine is unacceptable" (Noll, 2016). They are vital components of patient management and the healthcare system which helps in the allayment, management, and prevention of diseases.

Before the release of medicinal products to the market, they undergo various phases of clinical trials (Phase I-III) alongside strict regulatory guidelines and standards to ensure the medicinal products are of optimum quality, safety, and efficacy. However, during the trials, products are only tested on a limited sample size of patients with stated eligibility criteria, limited time, and used under the pre-decided protocol. These stated conditions make it impossible to detect long-term effects of drugs and their interactions, and rare ADR (ADRs) since the real world is not bounded by these protocols and conditions applicable to clinical trials. Also, drug safety information that is available after a drug has been approved, licensed, and released to the market is usually limited since the sample size of the patient involved in the clinical trial is small when compared to the real-world population of patients that requires the prescription of these drugs. Therefore, Post-marketing surveillance (phase-IV) which marks the commencement of pharmacovigilance activities is essential to detect and report all these adverse events and other drug-related issues that were previously not detected during the pre-marketing studies (Mishra and Dhikav, 2016).

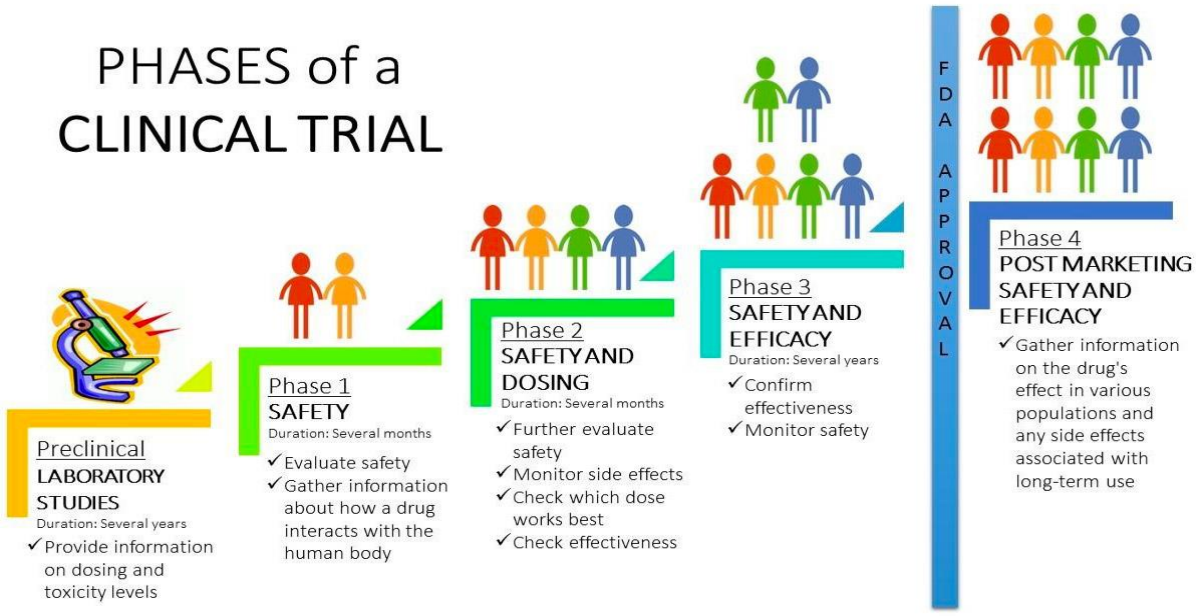


Figure 1: Phases of Clinical Trials sourced from (St. Luke's, 2020).

Evaluation and Monitoring of ADR

Monitoring of ADR through pharmacovigilance is essential to patient safety, and to ensure a good quality of human life and reduce the impact of ADRs on patients, as it is well known that no drug is free form adverse effects, therefore the need for continuous monitoring of drug and it is safety was introduced. According to World Health Organization (WHO, 2020), Pharmacovigilance can be defined as the *"science and activities relating to the detection, assessment, understanding, and prevention of adverse reactions or any other medicinal products related issues"* (WHO, 2020). The need for pharmacovigilance activities cannot be overemphasized as it helps in early detection of ADRs and identification of risk factors. It contributes significantly to the protection and sustenance of public health by promoting safe and effective use of medicinal products. The fundamental concept is to detect and prevent ADR in humans which may occur due to the usage of medicinal products before or after marketing authorization conditions (Nour and Plourde, 2019).

Assessment and spontaneous reporting of ADRs are vital methods for identifying new potential issues that are drug-related, and it is estimated that only about 6-10% of ARDs are reported which makes underreporting a major obstacle. Pharmacovigilance also aims to precisely optimize and identify medicinal products' benefit/risk ratio, effectiveness, and harm all through is life cycle, starting from discovery stage to post-marketing surveillance, and the mechanism underlying the ADR. The concepts of pharmacovigilance are dependent on these three pillars;

1. New information should be regularly obtained from reliable scientific resources such as HCPs, patients, market authorization holders, international/public agencies, etc.
2. Classification and assessment of the obtained information
3. The contents of the information and all actions taken will be circulated to all health sectors (Yadav, 2008).

The four elements that complete assessment and reporting of ADRs include- the drug, patient, an adverse reaction, and the reporter (HCPs). HCPs play a vital role in the pharmacovigilance system especially for early recognitions, detection, assessment, reporting, and management of ADRs. Therefore, they require considerable knowledge and expertise in the field of medication safety, which is why it is essential to improve the knowledge, attitude, involvement, and practices of HCPs towards ADR reporting and pharmacovigilance to address various challenges impacting maximum ADR reporting rate and optimum pharmacovigilance structure. Also, they are expected to consider ADR reporting as their professional obligation to

achieve an effecting reporting system which is paramount to improving patient safety and their overall health.

Similarly, the role of patients in reporting suspected ADRs can help add value and improve the efficiency of pharmacovigilance system. Patients should be encouraged to actively participate in the reporting system as they can describe their reactions in more details and the effect on their lives. They can help to generate new potential signals and provide useful information on likely causality, which will help bridge the gap of underreporting (Adisa and Omitogun, 2019).

Figure 2: Monitoring system of ADR sourced from (Yadav, 2008).

Causality Assessment of ADR

ADRs signals are reported information on potential causal relationships between a drug and an adverse event. There are several terms related to pharmacovigilance and this includes adverse events, ADR, and medication errors.

Adverse Event (AE) can be described as any harm that happens to patients during the use of a drug or other therapy, and the cause may not be directly related to the medicinal product or therapy being given.

Adverse Drug Reactions (ADRs) as defined by WHO is *"response to a drug that is noxious and unintended and occurs at doses normally in man for prophylaxis, diagnosis or disease therapy, or for the modification of physiological function"* (WHO, 2019). They are global problems of major concern that contribute to the high rate of morbidity and mortality across all age groups, and they also impose a major impact on the already strained healthcare system, and

substantial financial burden on society which greatly influences public health. Patients that are hospitalized due to ADRs incidence is estimated to be around 24.1%, and studies indicate that the death rate of patients who encounter ADRs is about 19.18% higher, and the duration of hospital stay is 8.25 % higher. It is often difficult to decide if an adverse clinical event is an ADR or it is due to the deterioration in a patient health condition, therefore a causality assessment is done to determine the causal relationship between the drug and their adverse reaction, to minimize the suffering of patients with ADRs (Gaurav Chhabra, 2017).

Causality Assessment is an integral part of ADR reporting and a common routine procedure in pharmacovigilance, it is performed to evaluate the relationship between particular drug treatment and the occurrence of an observed adverse event. It helps in signal detection of unusual and unexpected ADRs that were previously undetected during clinical trial evaluation of a drug. Also, it helps to better evaluate the benefit/risk of a drug profile to prevent future recurrence, while also helping the regulatory bodies to evaluate received ADRs report. There is a need for HCPs to be conversant with structured tools devised for causality assessment of suspected ADRs, and some methods to assess ADRs include:

- ***Clinical Judgement:*** This is usually performed by expert/HCPs by evaluating the ADR based on their knowledge and experience about the ADR.
- ***Probabilistic Approach:*** This method enables simultaneous assessment of multiple causes of ADRs, and the causality assessment is based on the study of prior and posterior probability.
- ***Algorithms:*** They are used to derive a structured and harmonized ADR assessment by classifying uncertainty in a semi-quantitative way to get the likelihood of causality. Naranjo algorithm and World Health Organization-Uppsala Monitoring Centre (WHO-UMC) are the most commonly used algorithm to assess ADR in this case.

Causality term	*Assessment criteria**
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon) • Rechallenge satisfactory, if necessary
Probable / Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional / Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable / Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

Figure 3: WHO causality assessment criteria sourced from (Gaurav Chhabra, 2017)

ADR can either be;

- Serious Adverse Reaction (SAR): This is when the reaction to the drug is serious and requires the patient to be hospitalized. It can be life-threatening, leading to disability, or even death.
- Unexpected Adverse Reaction (UAR): This is when the reported or detected reaction has not been previously stated in the medicinal product information or it is unpredictable with drug characteristics.
- Suspected Unexpected Serious Adverse Reactions (SUSAR). This majorly is a new side effect, it is when the reaction is serious and it is unexpected.

Over the years, ADRs are mainly classified as type A (dose-related) and type B (non-dose-related) reactions but other categories were added to the list over the subsequent years based on research conducted.

- ***Type A (Augmented):*** These are dose-related reactions and are usually related to the principal action of the medicinal product either through normal dose or overdose. They are common and mainly predictable from the known pharmacology of the medicinal product and skilled management can help reduce their incidence. It has both toxic and side effects and associated examples of this category include anticholinergic effects of tricyclics, digoxin toxicity, hypoglycaemia-insulin.
- ***Type B (Bizarre):*** These are non-dose-related reactions and are not related to the normal pharmacology of the medicinal product. They are less common, and any exposure is sufficient to trigger this type of reaction, also they are usually unpredictable, severe and might likely result in serious morbidity or even mortality. Associated examples of this category include anaphylaxis reactions, idiosyncratic reactions, and drug allergy.
- ***Type C (Chronic):*** These are dose and time-related reactions, they occur due to dose accumulation or long-term use of medicinal products and they are usually chronic. Associated examples of this category include Cushing syndrome from the use of corticosteroids for adrenal suppression, analgesic neuropathy,
- ***Type D (Delayed):*** These are time-related reactions in which drug does not accumulate but reactions manifest due to long-term use of medicinal product. Associated examples of this category include teratogenicity and carcinogenicity effects like tardive dyskinesia which occurs after a long period of using typical antipsychotics.
- ***Type E (End of Dose):*** These are withdrawal reactions that result from undesired effects of ending drug usage. Examples of this category include syndrome from opiate withdrawal and rebound hypertension after discontinuing usage of clonidine.
- ***Type F (Failure of Therapy):*** These reactions are used to illustrate undesirable reduction or increase in medicinal product efficacy. It occurs as a result of an unexpected failure of therapy in which a drug efficacy increases or decreases undesirably. Associated examples of this category include patient resistance to antibiotics which might lead to decreased effect of the drug, effects of critical ailment on elimination and protein binding, and other interactions of drugs that alter metabolism (Yartsev, 2019).

TYPE	TERM	CHARACTERISTIC	EXAMPLES
A	Augmented	Dose-dependent, Frequent, Predictable, related to the pharmacological effect of the drug.	Hypoglycaemia-insulin, bleeding after anticoagulants, Digoxin toxicity.
B	Bizarre	Dose-independent, Idiosyncratic ADRs, Unpredictable, Fatal.	Immunological reactions, Idiosyncratic reactions.
C	Chronic	Dose and time-dependent, Prolong toxicity exposure	Analgesic neuropathy, Cushing syndrome from cortisone.
D	Delayed	Time-dependent	Carcinogenesis, Teratogenesis, chronic organ damage.
E	End of Dose	Time-dependent, Relapse after the withdrawal of therapy.	Rebound or Relapse phenomena due to withdrawal effects of drugs i.e. Opioids or antiepileptic.
F	Failure of Therapy	Dose-related, Common, mostly occur due to drug interactions.	Inadequate dosage of an oral contraceptive,

Table 1: Classification of ADRs adapted by the author from (Edwards and Aronson, 2000).

Pharmaceutical Regulatory Affairs

Medicinal product regulations are the blend of legal, regulatory, and technical measures that are taken by assigned authorities/agencies to ensure the safety, efficacy, and quality of medicines, and also the pertinence, precision of the product details. It is of utmost importance to regulate pharmaceutical products in order to develop safe, quality, and effective medicinal products (Pierre-Louis Lezotre MS, 2014).

Pharmaceutical regulatory agencies play a vital role in the industry by ensuring the drug development process meets all applicable legal requirements to ensure the safety, quality, and efficacy of medicinal products available to the public. They aim to protect and improve public health and minimize accidents in the medical world by ensuring a great level of proficiency and control assessment is maintained, and preventing the penetration of counterfeit, harmful, and substandard products into the market. Also, they provide the strategic, tactical, and operational direction needed to promote the development and delivery of safe, quality, and effective medicinal products. Their functions and tasks range across all aspects of the industry

such as drug research and development, product registration, price control, manufacturing, marketing, distribution, and intellectual property protection. Furthermore, they implement and enforce laid down pharmaceutical regulations, guidelines required for medicinal product development, licensing, marketing, and labelling. Examples of the various regulatory agency in each country include; US Food and Drug Administration (FDA), European Medicines Agency (EMA) for Europe, Health Canada, Health Products Regulatory Authority (HPRA) for Ireland, Medicines and Healthcare Products Regulatory Agency (MHRA) for the UK, and National Agency for Food and Drug Administration and Control (NAFDAC) for Nigeria, etc. (Sengar and Tripathy, 2011).

National Agency for Food and Drug Administration and Control (NAFDAC) is a federal regulatory agency in Nigeria responsible for all medicinal products related affairs. It was established in January 1993 under a military decree which has now been amended during the democratic system to Act Cap N1 Laws of the Federation of Nigeria (LFN) in 2004 in order to control and regulate the manufacture, importation, exportation, advertisement, sale, distribution and use of drugs, medical devices, foods, cosmetics, chemicals, and all packaged water/drinks (NAFDAC, 2017). The national data bank of all reported ADRs in the country is coordinated by the National Pharmacovigilance Centre (NPC) which is a domicile in NAFDAC. There have been severe ADRs in Nigeria which has contributed to the high mortality and morbidity rate in the country and this include; error in the formulation of My Pikin teething powder which led to the death of 150 children, and the incidence of toxic paracetamol in 2008 which was adulterated with diethylene glycol and claimed the lives of some infants and young children. To reduce the burden of ADRs in Nigeria, NAFDAC has incorporated several measures to improve the quality of drug safety surveillance systems in Nigeria and ensure the efficacy, safety, and quality of all medicinal products.

Although Nigeria is currently participating in the WHO Uppsala monitoring program but their contribution towards the database is not up to the stated target and this can be attributed to lack of reporting culture among HCPs, and a listless ADR monitoring system.

Nigeria Healthcare System

The Nigeria healthcare system is divided into three levels namely- primary, secondary, and tertiary. The term tertiary is used to classify facilities owned by tertiary institutions or specialist centres that provide a full complement of medical services and medical care that requires highly specialized support functions, skills, and technology, usually for patients with uncommon, complex or rare severe medical conditions. They also serve as a referral centre for both primary and secondary centres, and they can be categorized into 3 different types which are:

- The Tertiary Institutions Teaching Hospitals- This category provides the underlying structure and teaching to HCPs during their undergraduate and postgraduate studies, it is also the best-suited category for research and healthcare services. The state of this research has most of the efficient teaching hospitals in the country which include- Lagos State University Teaching Hospital (LASUTH), Lagos University Teaching Hospital (LUTH).
- The Federal Medical Centre: This category provides healthcare services and residency training.
- The Specialist Hospitals: This category provides healthcare services in focused areas that are of public health importance, examples of this category in Lagos state include; orthopaedic hospitals (National Orthopaedic Hospital Igbobi), neuro-psychiatric hospitals (Federal Neuro-Psychiatric Hospital Yaba), St. Nicholas Hospital, Eko Hospital, Havana Specialist Hospital, etc.

Statement of Problem

Due to morbidity and mortality rate associated with ADR from the usage of medicinal products in Nigeria, the country needs to have a deep-rooted system for pharmacovigilance activities. The incidence of ADRs cut across all age groups with a large number of hospitalizations, as well as a high substantial financial burden on Nigeria society and it is healthcare system. Several cases such as Steven-Johnson syndrome, Nicolau syndrome due to dipyrone usage, the diethylene glycol incident from my pikin teething powder has negatively impacted public health (Olowofela *et al.*, 2016). It is estimated that only about 6-10% of ADRs are reported in Nigeria and several factors including slow involvement of tertiary hospitals, lack of awareness and knowledge of the reporting system and pharmacovigilance activity are stated to be a key factor. Also, the involvement of HCPs in the country is still quite laid back as most of them do not report a large proportion of the ADRs and this resulted in underreporting which is a crucial obstacle to spontaneous reporting of ADRs and poses a huge challenge to pharmacovigilance

activity. Nigeria lacks considerable knowledge and expertise in the pharmacovigilance field especially for early recognition, detection, reporting, and management of ADRs and this poses a great challenge to patient health and safety. Furthermore, lack of active patient involvement in the reporting system contributes to the underreporting as patients are major stakeholders in achieving spontaneous ADRs reporting which is a global phenomenon and the cornerstone of pharmacovigilance activity, therefore their impact needs to be evaluated and strengthened (Adisa and Omitogun, 2019).

Research Purpose

ADR present risk to patients' lives as they could significantly impact their lives by causing disability and mortality, and even cause an economic drain on healthcare system. A group of scientist once proposed that assessment of ADRs is likely the most essential part of drug therapy, and it helps in the identification of early signals related to the use of medicinal product, hence; active involvement of reporters contributes greatly to the success or failure of any spontaneous reporting system (Awodele *et al.*, 2018). This research is designed to explore how HCPs assess ADRs in tertiary hospitals. Also, this research will cover the passive surveillance method of pharmacovigilance which involves the spontaneous reporting of ADRs. It is a voluntary communication from HCPs or patients to regulatory bodies or the company that manufactures the medicinal product to help enhance post-marketing safety signals through identification, assessment, and reporting of ADRs. To effectively figure out and address the root cause of poor ADR reporting and suggest possible ways of improving pharmacovigilance structure in the aforementioned hospitals, this research will focus on tackling the slow involvement of tertiary hospitals in pharmacovigilance activities, and possible ways to impart knowledge regarding pharmacovigilance to HCPs, hence this research is designed to evaluate the following:

- Analyse the assessment and reporting process of ADR in tertiary hospitals in Lagos State, Nigeria.
- The impact of patients in reporting ADRs, and the attitude, perception of HCPs towards patient reporting ADRs in tertiary hospitals in Lagos State Nigeria.

Significance and Justification of the Study

The overall goal of this research is to analyse the assessment and reporting process of ADRs in tertiary hospitals in Lagos state, to figure out reasons for their slow involvement in pharmacovigilance activities. The previous research conducted on the pharmacovigilance system in Nigeria has been mainly focused on south-south and eastern healthcare system in the

country or been generalized, and their outcome shows several challenges and the need for improvement. Reviewed literature shows that extensive research has not been conducted in the involvement of tertiary hospitals, and the evaluation of the assessment of ADRs reported by HCPs in these hospitals. Furthermore, patients are a major stakeholder in fulfilling pharmacovigilance activities and spontaneous ADR reporting, but most research conducted has been majorly focused on HCPs and neglect the patients experiencing the ADRs; hence this study will also analyse the involvements and knowledge of patients in ADR reporting system. This research aims to recommend possible ways that can lead to spontaneous reporting improvement to fully integrate and maintain pharmacovigilance in the healthcare system.

This study will invariably contribute to the overall pharmacovigilance structure in place in tertiary hospitals by giving sustainable recommendations that will benefit both the hospitals and HCPs by increasing their awareness, help them identify and address the gap in the reporting system.

Aims and Objectives of the Research

The aims and objectives of this research are outlined below:

1) To assess the knowledge, attitude, and practice of HCPs towards Pharmacovigilance and ADR in tertiary hospitals in Lagos State, south-west Nigeria.
2) To elicit the experience of patients regarding reporting of ADRs and evaluate it is impact on pharmacovigilance structure.
3) To make sustainable recommendations towards patients reporting ADRs in Lagos state tertiary hospitals, which invariably will contribute to the overall pharmacovigilance system in place in the hospitals.

Research Questions

1. What are the assessment and reporting methods used by HCPs to identify and report ADRs in Lagos State tertiary hospitals?
2. What are the perceptions of HCPs towards patient reporting ADRs in Lagos State tertiary hospitals?
3. What is the level of awareness and knowledge of ADR among patients in Lagos state tertiary hospitals?
4. What are the challenges impacting ADR assessment, and responsible for the slow involvement of tertiary hospitals in Lagos state?

Hypothesis

Hypothesis One-

H0: There is no significant association between awareness of ADR and the identification of ADR.

H1: There is a significant association between awareness of ADR and the identification of ADR.

Hypothesis Two-

H0: There is no significant association between patients' source of knowledge on ADR and their ability to identify and report any experienced ADR.

H1: There is a significant association between patients' source of knowledge on ADR and their ability to identify and report any experienced ADR.

Hypothesis Three-

H0: Perception of HCPs has no impact on direct patient reporting of ADR in Lagos state tertiary hospitals.

H1: Perception of HCPs has an impact on direct patient reporting of ADR in Lagos state tertiary hospitals.

Scope of the Study

This dissertation will run across the assessment and reporting of ADRs in Nigeria and will focus mainly on HCPs and patients in Lagos state tertiary hospitals.

Structure of the Study

This dissertation is divided into five main sections which are introduction, literature review, research methodology, presentations and analysis of findings, and conclusions & recommendations. The first chapter begins with an introduction of research subject topic, it includes several subheadings such as; an overview of pharmacovigilance activities and ADRs, purpose of this research, significance and justification of research, and the aims and objectives of this research.

The second chapter which is the literature review presents the critical review of published research on pharmacovigilance activity, ADRs reporting system, healthcare professional involvement, and challenges that impact spontaneous ADRs reporting systems both in Nigeria and other parts of the world. Furthermore, it contains the conceptual framework which shows

the various elements and sub-elements that describe the concepts of assessment and reporting of ADRs.

The third chapter which is the research methodology includes strategy and design used to conduct this research. It discusses the methodological approach that the author has taken to meet her research goals and tackle her research questions. It also discusses her method of data collection which includes a mixed method of qualitative approach using phone interviews and a quantitative approach using questionnaires. Also, an Interpretivism and positivism research philosophy is used in this research alongside a deductive approach.

The fourth chapter which is the presentation and analysis of findings discovered, it discusses the data collected from both the interviews and questionnaire. Additionally, it interprets and explains the findings discovered as well as their impacts on research aims and objectives.

The fifth part which is the recommendations and conclusions discusses the summary and interpretation of the findings. It includes contributions and limitations of the research, recommendations for future research, practice recommendations. Furthermore, a final conclusion is drawn, and this relates all the information contained in the previous chapter and illustrates clearly how the research aims and objectives have been met.

Conclusion:

An analysis to evaluate the assessment of ADRs by HCPs and the impact of patients in the reporting system will invariably contribute to the overall pharmacovigilance structure in place in tertiary hospitals. It will provide a better insight into the loopholes and the various challenges encountered by HCPs in achieving spontaneous ADRs reporting. Furthermore, other measures such as adequate support and resources from applicable regulatory agency, increase awareness and visual displays of ADR reporting guidelines will serve as a constant reminder which will help lessen the burden of ADRs impact on patients' lives and the economy, and also improve HCPs attitude and perception towards pharmacovigilance and safety of drugs.

CHAPTER 2: LITERATURE REVIEW

2.1. Global Perspective

Medicinal products are the most common medical interventions primarily used in the treatment and control of diseases to relieve patient's suffering. But drugs have also been long recognized to prove fatal despite is medical intervention. Just as the popular saying that *"Drugs are double-edged weapons"* since they are likely to produce ADR from time to time (Shamna *et al.*, 2014). ADR are global health problem that requires the attention of all stakeholders regardless of the settings since it is a major limitation in providing adequate healthcare to patients at global level. Medicinal product usage differs after they are released to the market as compared to during their evaluation at the preapproval stages because they are used by a larger heterogeneous population. Hence, the establishment of an international drug monitoring program by WHO to create an active surveillance system to help monitor the safety of drugs and remove harmful drugs from the market (Shamna *et al.*, 2014).

The safety profile of medicinal products is dynamic, thus new information is continually assessed regarding it uses and outcomes through post-marketing surveillance. Post-marketing surveillance provides data that enhance the rational and safe use of a medicinal product, and out of the various methods involved in achieving it, national voluntary reporting systems are the most essential channel used for collecting and assessing information related to drugs adverse events. Pharmacovigilance is becoming a scientific discipline in it is own right since it plays a vital role in pharmacotherapeutic decision making, be it at the international, national, regional, or individual level (Yadav, 2008). Each country has it is specific coordinating pharmacovigilance program/unit that is responsible for gathering voluntary reports from HCPs and patients as regards ADR and other medicinal product-related errors. This program enables confidential reports of drug incidents and ADR needed for the provision of information to the public health community to optimize patient safety and to analyse data to detect potential issues and trends (Yadav, 2008).

Globally, the success of any pharmacovigilance system is based on several factors which include; adequate public awareness on the need to report suspected ADRs, viably trained HCPs, active communication system between regulatory agencies and public, fund, resources, and support from the government, Equipped quality control laboratories, Free flow of information such as feedback and inquires (Olowofela, 2018). As more drugs are produced and marketed, and patients take multiple drugs, the occurrence of ADRs is likely to increase. (Adisa and Omitogun, 2019).

2.2. Overview of Pharmacovigilance in Nigeria

World Health Organization (WHO) opined that Nigeria- located in the western region of Africa, and made up of 36 states including it is federal capital territory Abuja- is a developing African country and it is categorized as a lower-middle-income country (World Bank Group, 2020). It is a highly populated country with a current population of over 204 million people as stated by the world population statistics (Population Stat, 2020b) and has a diverse ethnic group.

According to WHO, it is estimated that the average life expectancy of a Nigerian is around 54.5 years of age, and this can be attributed to several tragic and striking health issues being faced in the country which also contributes to it is high mortality rates. Additionally, Nigeria has an infant mortality rate of 54.7% per 1000 live births, and it is approximated that out of every five children birthed in Nigeria, one is expected to die before clocking age five due to numerous health burden, risk, and issues faced by the country healthcare system. However, the country has been projected to have over 401 million populated by 2050 despite the death rate, and this is because Nigeria has a faster population growth rate of 2.6% which is significantly higher than other countries with the same size (Worldometer, 2020).

The journey of improving drug safety in Nigeria started in the 1980s with the involvement of is ministry of health by sponsoring some of their staff for training at the Uppsala Monitoring Centre. A major advancement in the history of pharmacovigilance in the country commenced in a tertiary hospital called University of Benin Teaching Hospital (UBTH) in the late 80s and early 90s when they set up an adverse reaction monitoring unit, established ADR registry, and drug/poison information centre (Olowofela *et al.*, 2016). Furthermore, the unit created a reporting system that generated sufficient spontaneous ADRs reports which facilitate the launch of the National Pharmacovigilance Centre (NPC) in 2003, and Nigeria admission into the WHO Program for International Drug Monitoring Programme (PIDM) in 2004 as the 74th member country of the program. This launched a new era for pharmacovigilance activity in the country (Opadeyi *et al.*, 2018). The country has sustained is activity through training it HCPs, general awareness and sensitization campaigns using electronic media and print about drug safety, and also the initiation of electronic devices to curtail falsified medicines and substandard drug products which is a major contribution to ADRs in the country. Pharmacovigilance growth in Nigeria has been propelled by several factors which include the establishment of NAFDAC in 2004, and the formulation of the Nigerian National Drug policy in 2005 which was further clarified in 2012 by the establishment of the Nigerian

pharmacovigilance policy document which strongly positioned drug safety in national discussion (Federal Ministry of Health, 2012).

2.3. Nigeria Pharmacovigilance Approach and Governance Framework

The National Pharmacovigilance Program in Nigeria was established with the objectives of monitoring the safety of medicinal products and creating an adverse reaction database for the Nigerian population. Nigeria has been mainly focused on ADR, counterfeit/falsified medicinal products, although the activity of monitoring and reporting ADR in the country is still in it is infancy (Opadeyi *et al.*, 2018).

According to Olowofela (2016), Nigeria has several tragic health and drugs related issues due to the burden of communicable and non-communicable diseases, poor recognition and quantification of morbidity and mortality rate associated with ADRs from using medicinal products. To establish a viable pharmacovigilance system in the country, NAFDAC's first step was the introduction of yellow forms in 2004 to help in early discovery and reporting of ADRs and to quantitatively evaluate the aspects of information dissemination and risk-benefit analysis essential for drug improvement. The five major components of the form include; patient's details, ADRs details, suspected drug details, concomitant details, and sources of reports (Awodele *et al.*, 2018).

Pharmacovigilance activities in Nigeria are coordinated at NAFDAC headquarters in Abuja by the National Pharmacovigilance Centre (NPC) which is a department of NAFDAC. Also, National Drug Safety and Advisory Committee (NDSAC) which consists of pharmaceutical and medical experts in the related field was inaugurated in 2006 to help provide expert advice on pharmacovigilance relevant issues. In 2012, the pharmacovigilance unit was separated from the Food and Drug Information Centre (FDIC) and upgraded to an independent directorate to manage all pharmacovigilance activities including post-marketing surveillance. Furthermore, zonal centres in six geopolitical zones in the country were established in 2013 based on WHO regional centres advocates, as these centres are an effective way to help facilitate the reporting system and enhance pharmacovigilance activities all over the country. Nigeria's objectives of establishing the zonal centres were to decentralize NPC activities and monitor the progress of pharmacovigilance activities at the institutional level. The zonal centres help to support capacity building and training for pharmacovigilance in the areas of their jurisdiction, help facilitate dissemination of information to patients and HCPs from the national centre, distribution of ADR forms and collection and evaluation of Individual Case Safety Reports (ICSRs) from reporters, and also acknowledgments and feedback conveyance to reporters.

NPC also works alongside several academic institutions and marketing authorization holders (MAH) which all have significant roles and contributions towards the development of drug safety in Nigeria in accordance with the developed pharmacovigilance policy (Olowofela, 2018).

Since NPC establishment in the country, it serves as a repository for reported ADRs and also liaise with applicable international organizations on pharmacovigilance activities such as World Health Organizations, European Medicines Agency (EMA), and US Food and Drug Administration (USFDA). The NPC centre in Abuja is responsible for collating, processing, evaluating, and handling ADRs reports in the country, the reports are evaluated and verified according to WHO criteria before they are sent to WHO Uppsala monitoring centre using VigiFlow software and stored in VigiBase data system. NPC actively promotes and focuses greatly on the necessary steps required to transform and implement an ideal framework to fulfil ADR obligations. Guidance documents and reporting forms were established by NPC to promote an efficient reporting system among Market Authorization Holders (MAH) and HCPs in the country. Furthermore, they created a reporting Pharmacovigilance Rapid Alert System for Consumer Reporting (PRASCOR) to encourage patient's contributions towards pharmacovigilance reporting system in Nigeria, this utilizes text messages to report ADRs directly to the NPC for evaluation. All the measures put in place are to increase awareness about pharmacovigilance, bring a centre closer to the practice of reporters, and instil a sense of ownership among the stakeholders as regards pharmacovigilance activities. (Olowofela *et al.*, 2016).

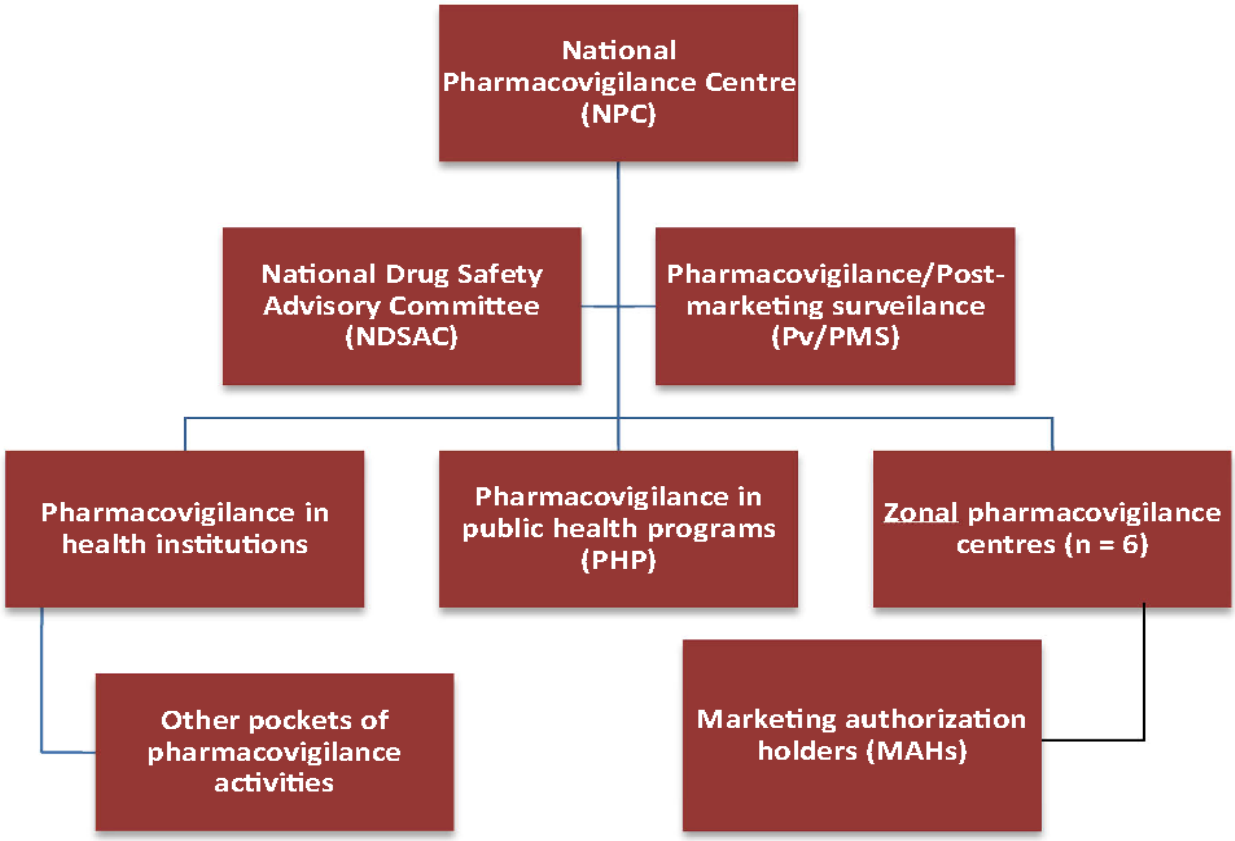


Figure 4: Pharmacovigilance operating system in Nigeria, sourced from (Olowofela et al., 2016)

2.4 Pharmacovigilance Activity and ADR Reporting

Pharmacovigilance activity is an essential part of drug therapy which helps in detection, monitoring, identification of risk factors, designing strategies to help reduce ADRs occurrence, and dissemination information. The scope of pharmacovigilance is wide with increasing product concerns, and it is not only limited to drugs but has now been expanded to other products such as medical devices, biologics, vaccines, blood products, and herbal products (Yadav, 2008). Pharmacovigilance involves actions to detect and assess ADR, and evaluation of the probability of the association within the drugs and the ADRs. It includes the consistent monitoring of drug safety and reporting of ADR of medicinal products that are already available in the market, most especially during post-marketing surveillance. These surveillance activities are very essential to enable the early detection of unexpected and/or serious ADR and assure the safe use of drugs. Pharmacovigilance is the principal unit control of the menace of ADR, and it importance in therapy outcome is essential and crucial for effective clinical practice and public health science (Oreagba *et al.*, 2011). In particular, Pharmacovigilance effectiveness and success are directly dependent on the involvement of HCPs and patients (according to new European Pharmacovigilance Legislation) through their prompt and frequent

reporting of suspected ADR as under-reporting can have a negative impact and disadvantages (Palleria *et al.*, 2013).

A study by (Kaur *et al.*, 2019), titled pharmacovigilance study of ADR in a tertiary care hospital in Haryana retrospectively analysed a total of 233 ADRs reports from various department of the hospital. The authors established that more ADRs were noted in females which is 133 making about 53% of the patients studied, and 100 was noted in males which is about 43% of the patient studied. Furthermore, the authors established that the highest reported ADRs were from the dermatology department with a case of 60 making 25.8%, followed closely by the surgery department with a case of 54 making 23.2%. Several organ systems were affected by ADRs and this includes- The skin which was the maximally affected area noted 154 making about 70%. Followed by the gastrointestinal system which noted 28 making about 13%, and the other organ system such as the central nervous system, immunological, endocrine, respiratory, and cardiovascular make up the remaining 17% (Kaur *et al.*, 2019).

Organ system	ADR	Number	Organ system	ADR	Number
Skin	Rash/urticaria	80	**Central nervous system**	Restlessness	07
	Dermatitis	42		Headache	01
	FDE	16		Tremor	01
	TEN	01		Dizziness	06
	Erythema	06		Psychosis	01
	Exanthema	01		Vertigo	01
	Lichenoid-eruptions	02		Seizure	01
	Pemphigus vulgaris	01		Nocturnal enuresis	01
	Psoriatic erythema	01	**Immunological**	Chills and rigors	06
	Echymosis	01		Drug hypersensitivity	01
	AGEP (acute generalized exanthematous pustulosis)	01		Flare of infection	01
	Dryness of skin	01		Angioedema	13
	DRESS (drug rash with eosinophilia and systemic symptoms)	01	**Endocrine**	Amenorrhea inhibited orgasm	02 01
Gastrointestinal	Vomiting	10	**Musculoskeletal**	Periorbital edema	01
	Diarrhea	02	**Ophthalmology**	Congestion in the eye	01
	Bitter taste	01	**Peripheral nervous system**	Tingling and paresthesia	02
	Gastritis	04	**Respiratory**	Cough/dyspnoea	02
	Oral ulcer	04		Respiratory distress	01
	Nausea	07	**Cardiovascular**	Hypotension	01

Figure 5: Organ system involvement due to ADRs, sourced from (Kaur et al., 2019)

2.4.1. Current State of ADR in Nigeria

Global drug safety greatly depends on a strong national system that monitors the development and quality of medicinal products, assesses and reports their harmful effects, and provides accurate information for their safe use (Palleria *et al.*, 2013). Medicinal product usage, patterns, and the nature of common diseases, disease burden, and cultural norms that can influence the

assessment and reporting of ADR are unequally distributed among high and low-income countries. It has been established that developed countries use more drugs and they have greater resources in terms of infrastructure, money, and competency to survey the safety of medicinal products. Aagaard et al. stated that there is extensive information about ADRs occurrence in high-income countries especially from USA and Europe, but there has been only limited data about ADRs occurring in low-income countries. However, the safety of medicinal products at a global level needs more information and it is essential to determine if the occurrence of reported ADRs is associated with national wealth (Aagaard *et al.*, 2012). A study that analysed ADRs reported to WHO VigiBase for antimalarial medications established high reporting rates from high-income countries than low-income countries despite the huge malaria cases in low-income countries. There were wide variations in reporting rates between country income level and this can be attributed to the fact that high-income countries have a well-established and long-term pharmacovigilance system and resources (Aagaard *et al.*, 2012).

There have been significant literature reviews of ADRs observed in Nigeria populations due to drug quality issues, polypharmacy, high usage of herbal medicines, free medicines given at public-health programs, and this has been reported to contribute to the rate of ADRs in the country (Olowofela *et al.*, 2016). According to a survey carried out on the Nigerian market, the survey revealed that about 48% of the drug tested did not conform to international pharmacopeia standards. This incident led Nigeria pharmacovigilance activity to be majorly focused on ADRs as well as SSFFC (Olowofela *et al.*, 2016).

Unfortunately, despite the long existence of pharmacovigilance in Nigeria, NPC is yet to achieve the expected recommendation of 200 reports per million population target by WHO and this may be attributed to several factors such as declining health care standards, insufficient expertise in pharmacovigilance, increasing population burden, poor framework/infrastructure set-up, inadequate funding and resources dedicated towards pharmacovigilance, poor recognition of ADR, lack of focus and dedication towards pharmacovigilance by required parties/personnel, ADRs bulky/inefficient reporting process, and under-reporting from HCPs which contributes negatively to the feedback received by NPC (Olowofela, 2018). This is not only specific to Nigeria as other reviewed research on pharmacovigilance in other Africa countries shows pharmacovigilance activity is underappreciated due to similar issues especially insufficient expertise, lack of political goodwill, and poor funding contributes to the limitations. Unfortunately with the declining healthcare standards and increasing population burden over the years, only a notable drug-related event has been recorded as opposed to the burden of

ADRs that occur in the country, and this highlights the need to improve and be more focused towards pharmacovigilance in Nigeria healthcare system (Olowofela *et al.*, 2016).

2.4.2. Assessment and Reporting of ADRs in Hospital Settings

ADR are frequent occurrence in hospital settings, and this can be attributed to several factors such as; complexity and severity of the disease, over-enthusiastic prescription, polypharmacy, drug interactions, and possible negligence. ADRs may be observed in about 10-20% of hospitalized patients, therefore hospital-based ADR monitoring and reporting programs can help identify and assess risk associated with drug usage. It is important to establish a systemic manner for assessing drug safety in hospital settings by having active surveillance, collection, and assessment of data regarding drug incidence, severity, and type of adverse events. Although accurate data are useful but measuring the incidence, nature, and severity of ADRs to a drug is not enough, it is also essential to assess patterns of ADRs against each other to identify their impact on patient lives (Gor and Desai, 2008).

Due to the type of treatment offered in tertiary hospitals, most ADR evidence and cases arise from these settings because of the high risk associated with their treatments. A study conducted in USA by Agency for Healthcare Research and Quality (AHRQ) in 2011 established that causative relationship revealed that most frequent causes of an adverse event that occur during hospital stay were as a result of antibiotics, steroids, anticoagulants, and narcotics/opiates. It established that patients treated in tertiary hospitals have higher rates of adverse events as compared to patients treated in non-tertiary hospitals due to the type of therapy and drugs administered to them (Akhideno *et al.*, 2019). Since diagnostic tests are often absent and re-challenge is barely ethically justified, it is usually difficult to recognize if a clinical event is an ADR or it is due to the deterioration in the patient's primary condition. Hence, it is important to identify ADRs and demonstrate a causal relationship between the medicinal product and the untoward clinical event, although there are scales like the visual analogue scale that help physicians assess the severity of ADRs. Likewise, some vital factors can help to adequately recognize and assess causation. This includes; patients with certain health conditions like liver and renal dysfunction, Human Immunodeficiency Virus (HIV), patients in polypharmacy, and premature and aged patients (Doherty, 2009).

According to a publication by Doherty (2009) on assessing probability of an ADR, the author established that ADR assessment was previously based on clinical judgment alone, but it is recognized that individual judgment may differ and that the semantics of the definitions are critical. This led to the development of several algorithms/decision aids to help improve the

scientific basis of causality assessment and reduce the disagreement between assessors. Algorithms were developed during the 70s and 80s, they provide standardized methods that help in recognizing ADR since they are structured system that is explicitly designed to facilitate ADR identification (Doherty, 2009). Their main advantage is associated with the feasibility of decentralizing causality assessment from medical diagnosis and extending it to different healthcare level i.e. pharmaceutical industry, academics, and health agencies. It is important to consider the method of assessment used for assessment before validating an ADR report even though the quality of data and documentation influence the method reliability (Satyen, 2013).

Furthermore, the status of pharmacovigilance system in tertiary centres is unknown as regards it is effectiveness and functionality because the WHO indicators and related metrics for assessing these hospitals have just been newly published. In a study titled assessment of the state of pharmacovigilance in the south-south zone of Nigeria using WHO pharmacovigilance indicators by Opadeyi et., al (2018); the study was carried out in six tertiary institution hospitals in south-south Nigeria using a modified WHO data collection form to obtain the data. The data were analysed using both quantitative and qualitative methods based on WHO pharmacovigilance indicators. The authors established that one of the hospitals called UBTH performed better at the assessment as compared to other hospitals even though there was a general pharmacovigilance acceptance and structures were gradually put in place despite institutional challenges. Additionally, it was revealed that the processes and outcomes indicators were poor in all the facilities which was attributed to lack of awareness of measuring indices to monitor and evaluate pharmacovigilance, insufficient manpower, poor budgeting for pharmacovigilance, and poor record-keeping as regards routine data gathering and documentation of ADRs and other medicines-related events, (Opadeyi *et al.*, 2018).

The incidence of ADRs among hospitalized patients in the United Kingdom was stated around 6.5% and admissions related to ADRs cost the national health scheme up to £466 million annually (Akhideno *et al.*, 2019). Also, McKinsey & Co in 2012, established that 35 million preventable adverse drug events cost would be as high as the US $115 billion (Mckinsey, 2012). Assessment and reporting systems of ADRs need to be robust and complete to be able to detect possible signals, new drug alerts, and improve the pharmacovigilance system. But the pharmacovigilance structure in most hospital settings is still in their infancy and the requisite culture to ensure effective operations is yet to be established. Therefore continuous ADR monitoring and causality assessment is essential in this settings as it can help to facilitate early

recognition of ADRs, reduce hospitalization stay and unnecessary burden associated with it, establish barriers to prevent ADRs recurrence and unexpected/serious drug effect, and in general improve the quality of patient treatment and their lives (Varallo *et al.*, 2017).

2.4.3. Completeness of Submitted ADRs Report

In 1960s, WHO established a system to collect information about suspected ADR and this has been equally established in many countries by their respective pharmacovigilance centres. Unfortunately, despite the stated process, the incompleteness of submitted ADRs report to pharmacovigilance centres remains a global problem that hinders the effectiveness and complete evaluation of submitted ADRs report for drug causality.

According to a publication on patterns of ADRs signals in NAFDAC pharmacovigilance activities by (Awodele *et al.*, 2018), the study analysed a total of 935 reported ADRs for 6 months and only 509 reports were complete and others have missing information such as the ADR start/stop date, suspected drug used, and other relevant requirement needed to validate the form. The outcome of the study was consistent with other published research on incompleteness of submitted ADRs reports to pharmacovigilance centres in countries like Saudi Arabia, Italy, and Mexico. The study suggested timely evaluation of received suspected reports for early detection of incomplete reports, and reporters should be reached and encouraged with incentives to facilitate sufficient and complete reports since NPC has no rejection policy for incomplete reports (Awodele *et al.*, 2018).

Completeness of spontaneous ADR reports submitted by general practitioners to a regional pharmacovigilance centre in Toulouse, France from 2010 to 2013 was analysed by Durrieu et al. (2016). The authors established that only 12.7% of the reports were classified as a well-documented report using multivariate logistic regression to investigate potential factors associated with a well-documented report. While 68.5% were slightly documented and 18.8% were poorly documented (Durrieu *et al.*, 2016). Pharmacovigilance awareness for patients and training for HCPs should promote and emphasize the importance of completing an ADR reports forms regarding relevant data when reporting it, in order to optimize the evaluation of drug causality.

2.5. Role of HCPs (HCPs) in Assessment and Reporting of ADRs

The fundamental role of HCPs is to identify potential and actual medicinal products related issues, resolve them, and prevent reoccurrence. HCPs are encouraged to be actively involved in the monitoring, assessment, and reporting of ADRs to strengthen pharmacovigilance practice

and ADRs awareness, increase opportunities to review drug selection and incorporate sense of ownership. Since patients' needs are changing, shifting from diagnosis and single acute problem treatment to long-term management of several interrelated chronic health conditions. HCPs need to adopt new parameters to proactively survey and monitor ADR continuously and integrates patient's safety as core value and practice (Shewale *et al.*, 2009). They are major stakeholders in achieving spontaneous ADRs reporting since they prescribe and follow up on treatment outcomes, thus they are best suited to detect ADRs based on the information gathered from their clinical observations and patients. HCPs have to ensure patients are aware of the risk of side effects and a suitable course of action in case they occur, but since reporting is based on voluntary participation, they are limited by under-reporting and a variance in quality of report received (Sriram *et al.*, 2011).

The involvement of tertiary hospitals is still quite slow in the implementation of most of the objectives stated in the pharmacovigilance policy, and there are fewer experts in the field which contribute significantly to the retarded growth of pharmacovigilance activity in the country. This is because the responsibility of reporting ADRs in these hospitals is majorly considered to be doctor's responsibilities since they are regularly reasoned to be the first among the list of ADRs primary reporters. Other HCPs such as pharmacists and nurses withdraw from this responsibility as they are less involved with patient management in tertiary hospitals, hence they feel less obligated to report ADRs. In contrast, nurses are more involved with patient management in primary health centres as well as pharmacists practicing in community pharmacies, they are in a privileged position to detect ADRs and even educate patients on the reporting process because of the direct contact they have with them. Considering the numbers and easy accessibility of primary health centres and community pharmacies in Nigeria, the influx of patients in these centres can significantly contribute towards better spontaneous ADRs reporting (Adisa and Omitogun, 2019). Furthermore, the role of pharmacists to become active stakeholders in the detection and reporting of ADRs has undergone profound changes over the last few years, especially in pharmacotherapy outcomes through the provision of comprehensive medication review services, and in encouraging direct patient reporting (Inácio *et al.*, 2018).

Error-free performance and great expectations are standard expected from HCPs, but the health system and personnel are not fail-proof, so errors are made with high human and economic costs. Lack of awareness, interest, time, aptitude, clinical acumen, confidence, and experience with assessment and reporting of ADRs has made lots of untoward adverse incidents pass

unnoticed, and this is a major deterrent that contributes to their slow/inactive involvement (Sriram *et al.*, 2011).

Additionally, the role of HCPs is important in correct drug usage, therefore their participation requires awareness and knowledge of pharmacological therapy, toxic profile of administered drugs, and drug product characteristics- such as warning, indications, and contraindications. This is critical to observe an ADR for proactive monitoring and reporting, and also a careful assessment of patient's history and health condition can help prevent most ADRs associated with inappropriate prescription (Shewale *et al.*, 2009).

2.6. Reporting of ADRs by Patients

For several years after the establishment of the ADR reporting system in the 1960s, only doctors could report ADRs. However, that changed over time has patients, pharmacists, and other HCPs are now allowed to report ADRs, even though some countries have still not accepted patient reporting in their national reporting programs (Aagaard *et al.*, 2012). The history of patients reporting ADRs can be traced back to 1983 when it was first considered by a working party of the Committee on Safety of Medicines (CSM) after the withdrawal of benoxaprofen. In 2000, possible benefit is of patient reporting were summarised at the first international conference on consumer reports on medicines, which consists of the promotions of patients' rights and equity, acknowledging that patients have unique experiences and perspectives, and their involvement would be beneficial to healthcare organizations. ADRs could cause significant disability, morbidity, and mortality risk to patients' lives therefore patients need to be encouraged and engaged actively in reporting ADRs, as monitoring and reporting of adverse drug reaction is vital to their safety. The new pharmacovigilance legislation in the European Union introduced several changes which include the formal implementation of patient reporting, and this had led to the implementation of patient reporting systems in several countries (Inácio *et al.*, 2018). Furthermore, it is widely known that underreporting of ADRs by HCPs is a substantial issue that needs to be addressed effectively, thus adding patients to the pool of potential reporters will help in earlier detection of significant ADRs, and boost spontaneous reporting (Avery *et al.*, 2011).

According to a research titled "*evaluation of patient reporting of adverse reactions to the UK Yellow Card Scheme (YCS)"* by (Avery *et al.*, 2011), the study was carried out with submitted yellow card reports from patients (n=5180) and HCPs (n=20,949) from October 2005 to September 2007. The authors established that about one-third of their respondents expected feedback and motivations for reporting from the regulatory agency, while a few of them made

comments about HCP lack of awareness and dismissive attitude towards ADRs. A few of them stated that HCPs were unaware of patient reporting ADRs, discourage them from reporting, and refused to make a report on their behalf. Furthermore, the authors established that patients report described a more detailed reaction than that of HCPs, and it contained a higher median number of suspected ADRs per report, even though it was just 8.5% of the public population that were aware of the YCS. This report provided useful information on likely ADRs causality and impacts on patients' lives, and also the outcome stated that the combined reports of patients and HCPs helped identified 47 new serious reactions that were not previously included in the Summaries of Product Characteristics (SMPC) (Avery *et al.*, 2011).

Another publication titled adverse drug reaction reporting in the UK; A retrospective observational comparison of yellow card reports submitted by HCPs and patients, the study analysed a total of 26, 129 yellow card reports from both HCPs (80.2%) and patients (19.8%) to compare patient characteristic and their report on suspected ADRs and suspected drugs with that of HCPs using the yellow card scheme. The authors established that the quality of reports of both HCP and patients were similar, and patients reported a higher proportion of suspected drugs and suspected ADRs than that of HCP -16.1% vs 9%, while HCPs mostly reported ADRs that are life-threatening (11.1 vs 6.2%), hospitalization (18.8% vs 12.9%) or caused death (2.6% vs 0.7%) than patients (McLernon *et al.*, 2010).

Unfortunately, just like HCPs, patients experience similar barriers such as insufficient awareness, uncertainty about responsibility for reporting, and lack of feedback for submitted reports. Providing continuous educational activities, dissemination of information in accessible language through HCPs or patients organization, and culture of simplicity and eliminating reporting barriers need to be aimed at and promoted by relevant authorities to actively integrate patient reporting (Inácio *et al.*, 2018). A combination of both HCPs and patient reports can help generate more potential signals as compared to reports only from HCPs, and bridge the gap of underreporting on the part of HCPs. Patients are a major stakeholder in achieving spontaneous ADR reporting, and the true value of them reporting ADRs directly will remain unknown until more studies and evaluations are conducted.

2.7. Perception of HCPs Towards Patients reporting ADR

Healthcare professional's perceptions towards patient reporting ADRs have not been extensively studied globally, only a few research has been conducted in countries such as Malaysia and UK, while other countries including Nigeria is yet to explore and evaluate the perceptions of it is HCPs towards direct patient reporting.

In a publication titled do health professionals have positive perception towards consumer reporting of ADR by Alshakka et al. (2013); The study was carried out using a cross-sectional mail survey to 104 participants which include 57 general practitioners and 47 community pharmacist in Penang island, Malaysia. The authors established that 88% of the participants agreed that patients reporting would contribute significantly to the existing pharmacovigilance program, and 97% also agreed that patients need more education regarding reporting of ADR. However, the authors stated that 68% of the participants were not aware that patients can report ADRs in Malaysia, while about 84% thought that patients cannot write a valid report as that of the HCPs (Alshakka *et al.*, 2013).

Another publication titled views of British community pharmacists on direct patient reporting of ADRs by krska (2013); the study was carried out using a questionnaire among 297 community pharmacists in the UK. The author established that 85.2% of the respondent was aware of patient reporting, but only 57.9% had an accessible patient reporting form, while only 18% displayed a promotional poster to facilitate patient reporting ADRs. The study also established that the majority of the respondent prefer the reporting process to be restricted only to HCPs. The respondents will rather do the reporting themselves than informing their patients about direct patient reporting because they feel patients need help to complete their medical history, and the yellow card form is too complicated for them to fill. Only 14% indicated they would create more awareness about patient reporting, and encourage their patient to report directly (Krska, 2013).

Studies have shown that HCPs are pessimistic about the success of patient's direct reporting of ADRs. HCPs believe that patients do not have sufficient knowledge regarding their medicines and hazards, therefore they can't produce quality information on ADRs nor generate a valid report. HCPs believe that ADR reporting is meant to be strictly restricted to them and patients are only meant to report ADRs through their healthcare providers. The above-mentioned views are still a barrier that needs to be extensively studied all over the world.

2.8. Limitations of Assessment of ADR in Nigeria

The main purpose of assessment and reporting is to enable rapid detection of potential signals related to drug use and identify rare and serious ADRs that may occur after drugs are marketed. However, there are well-known limitations such as variable quality of reported data, poor recognition of ADRs, underreporting, lack of information on drug exposure, and inability to use spontaneous ADR reporting to determine incidence or prevalence of ADRs since the characteristic of drug usage is unknown (Aagaard *et al.*, 2012). Also, missing data and

incompleteness of submitted reports to pharmacovigilance centres is a significant limitation, especially in developing countries like Nigeria.

In developing countries like Nigeria, there is minimal information on the in-hospital incidence of ADRs, and the culprit medications, this is because the assessment and reporting medium in Nigeria is inadequately efficient and somehow being underutilized by Nigerians including the HCPs and healthcare providers. HCPs sometimes do not report ADRs because they find it challenging to establish with certainty the potential causal relationship between a drug and an adverse reaction (causality assessment). However, according to a vital principle of pharmacovigilance, it is important to report even suspicion to generate an alarm in the interest of protecting public health (Palleria *et al.*, 2013). Additionally, this information is useful for health management, planning, budgeting, formulation of policy, and for the development of treatment protocol required to ensure appropriate and optimal patient care (Akhideno *et al.*, 2019).

The aim of institutionalizing pharmacovigilance in Nigeria healthcare facilities both at state and federal level is still the main objective that is yet to be achieved, there is need for more capacity building to viable train HCPs on assessing suspected ADRs. Also, there is need to categorize and assess the ADRs related to herbal medicines which are broadly used by the Nigerian population. Furthermore, lack of active patient involvement in the reporting system contributes to the underreporting as patients are major stakeholders in achieving spontaneous ADRs reporting which is a global phenomenon and the cornerstone of pharmacovigilance activity, therefore their impact needs to be evaluated and strengthened (Adisa and Omitogun, 2019).

2.9. Conclusion

Following a comprehensive review of published articles and papers, it is obvious that ADR reporting and assessment culture are not well established as depicted by the huge gap between encountered ADR and it is reporting trend among HCPs. Although HCPs have a positive attitude towards assessing and reporting ADR, however, they have poor knowledge and practice towards it, hence ADR workshops and training should be conducted worldwide to provide guidance and update their knowledge, while good pharmacovigilance practice should be developed according to international standards. Pharmacovigilance systems are essentials and their knowledge could be further improved, therefore increased institutionalization of pharmacovigilance and improvement in medical record documentation should be incorporated into pharmacovigilance activities in tertiary hospitals. Furthermore, patients should be

educated and engaged as regard reporting of ADRs, as this will help achieve a better spontaneous report, generate possible signals, and reduce ADRs that could have otherwise been prevented.

Since ADRs are unavoidable risks associated with medicinal products, it is essential to develop an effective process for it is assessment, monitoring, and reporting process to invariably contribute to the overall pharmacovigilance structure in place in Nigeria and other parts of the world.

2.10. CONCEPTUAL FRAMEWORK

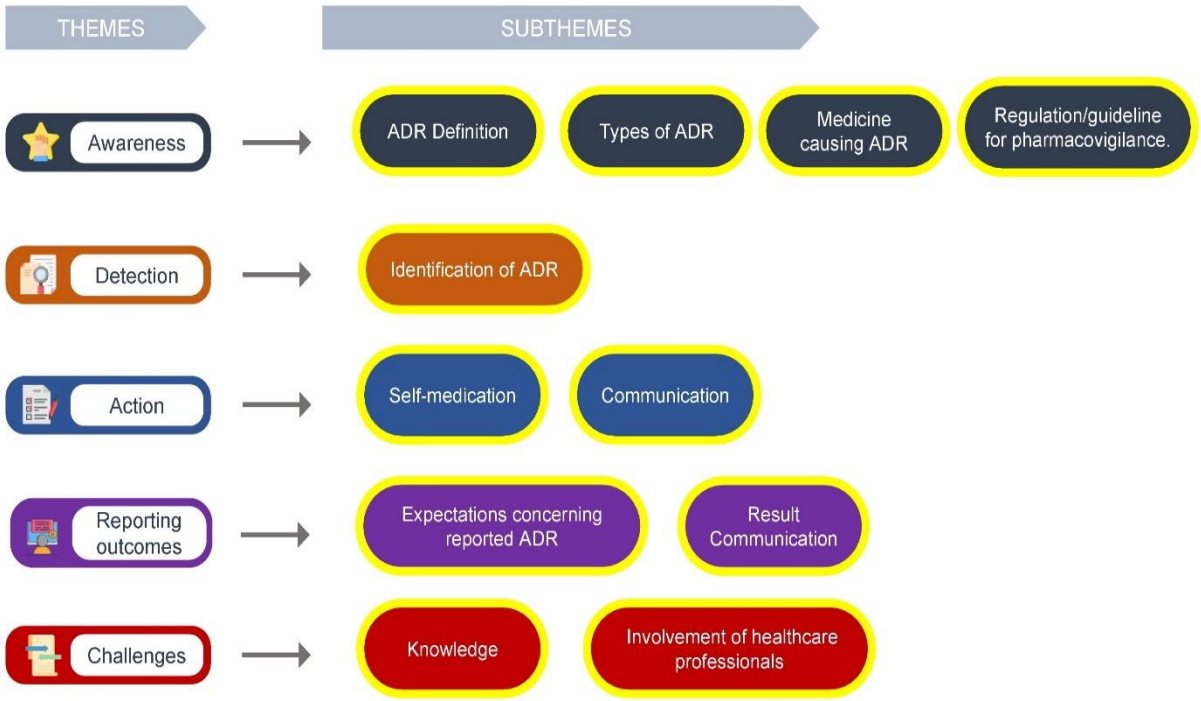


Figure 6: research conceptual framework, created by the author

CHAPTER 3: RESEARCH METHODOLOGY

3.1. Overview

This dissertation was modelled on a mixed-method research methodology which includes qualitative and quantitative methods, it was based on the use of deductive survey questions. The researcher chose mixed-method to overcome the constraints of a mono-method by using the qualitative data to complement her quantitative data. The study was exclusively conducted among HCPs and patients in tertiary hospitals in Lagos State metropolis, Nigeria.

PHASE	PRIMARY DATA	RESEARCH PARAMETERS PART 1	RESEARCH PARAMETERS PART 1
1.	Methodology	Quantitative	Qualitative
2.	Philosophy	Positivism	Interpretivism
3.	Selection Criteria	Medical doctors, Nurses, Pharmacist, and Patients in tertiary hospitals	Medical doctors, Nurses, and Pharmacists in tertiary hospitals.
4.	Data Collection Source	Highly structured questionnaire	Semi-structured phone interviews
5.	Structure	5 sections which consist of 21 questions	10 questions which lasted for 30 minutes on average.
6.	Sampling Technique	Random sampling	Purposive/Snowballing sampling
7.	Sampling Frame	450 participants targeted; 405 response was successfully obtained	6 highly experienced HCPs

Table 2: Overview of research design and primary data collection created by the author

3.2. Research Study Setting and Population

Lagos is the largest populated state in Nigeria and in sub-Saharan Africa state in the south-western geopolitical zone of Nigeria, it has a current population of over 14 million people in it is cities and urban areas. The state has five administrative divisions which are further divided into 37 local government areas (Population Stat, 2020a).

Based on Healthcare Facilities Monitoring and Accreditation Agency (HEFAMMA) statistics, Lagos state consists of 26 registered general hospitals, 256 public health centres, and 2,886 specialists/private hospitals. It has one of the most efficient healthcare systems in the country based on the high numbers of primary, secondary, and tertiary centres present in the state. This study was focused on all categories of tertiary hospitals in Lagos state because these hospitals have the widest access to all cadres of HCPs and patients which helped the researcher to get diverse data on spontaneous ADRs assessment and reporting.

3.3. Research Approach

As shown in the table above, the researcher used a mixed-method approach to gather her primary data, which includes; quantitative approach using a questionnaire to collect relevant data from a reasonable number of HCPs and patients, and a qualitative approach using phone interview to explore information from a selected number of highly experienced HCPs to support her findings.

The quantitative approach was aimed at obtaining insight from the practice of HCPs towards direct patient reporting, and ADRs assessment and reporting process. And to also obtain applicable information from patients as regards their knowledge and awareness on ADRs reporting. This was facilitated through the use of an electronic survey that generated rich descriptive data from the participants while eliminating any risk of bias, influence, and maintain minimal interactions with them. On the other hand, the qualitative approach was aimed to draw out insights and explore in-depth information from the practice of selected HCPs on their perception towards direct patient reporting, and the assessment and reporting of ADRs in Nigeria tertiary hospitals. This was facilitated through a semi-structured phone interview which led to the generation of in-depth explanatory data. The combination of these two approaches enabled the researcher to gather a wealth of data that was used for quantifiable measures for statistical analysis.

The questions were drafted in a way that has a feel of the human element to understand the perceptions of HCPs towards direct patient reporting ADRs and establish awareness about the

existing assessment and reporting process in tertiary hospitals. Also, the researcher ensures her questions were addressing the most important issues in her research study, which enabled her to propose feasible recommendations and improvements that will invariably contribute to the overall pharmacovigilance structure in place in tertiary hospitals which can be sustainable over a long period.

A deductive approach was used rather than an inductive approach because the concepts of this study were operationalized in a way that enables facts to be measured quantitatively while ensuring clarity of definition. This approach enabled the cause-effect link between findings, and the researcher was independent of what was being observed (Saunders *et al.*, 2009). It also helped ensure reliability and validity of data, and envisage the certainty of this study through the application of controls. After the analysis of the data collected from respondents, the findings were compared to other applicable literature in the field and public views to check that they are in-line and in agreement with the already established norms and to clearly express the researchers concluding view on the research being conducted.

3.4. Research Philosophy

The fundamental philosophy of this research is a Positivism and Interpretivism, it was implemented for this study to obtain quantifiable observation which was useful for statistical analysis of information gathered from participants, and to derive an appropriate conclusion. The positivism philosophy helped facilitate replication of response from respondent through the use of a highly structured questionnaire which was distributed electronically to the group of participants. The researcher was independent of what was been observed and only concentrated on the fact available without any human interference or bias within the study. The research progress through hypothesis that required the use of large randomly selected samples of HCPs and patients which were easily measurable.

The usage of Interpretivism philosophy for the qualitative approach was due to the subjectivity involved since all participants selected for the interview process had different perspectives about ADRs assessment and reporting practice. Also, several factors such as their services, process, patients size, and policy on pharmacovigilance had an impact on their reporting system, and this helped to frame the information obtained via phone interview which resulted in data that was shaped by their individual interpretation, values, and perspective of reality based on their experience and belief.

A combination of descriptive and explanatory research was adopted for this research to gather information from 411 respondents via online survey and telephone interview. For the descriptive research, the researcher identified and described the variability in different phenomenon without any form of bias or interference with the data gathered through analysing the perception of HCPs towards direct patient reporting of ADRs, and towards the assessment and reporting process in their hospitals. Also, it analysed patient knowledge and awareness as regards the ADR reporting. For the explanatory research, the researcher examined and explained the relationship between the variables such as opinion, behaviour, and attribute variables of the respondents.

3.5. Research Strategy

To fulfil the research objective, a mixed-method approach was used. The strategy of this research was to analyse the perception of HCPs towards direct patients reporting ADRs and the assessment and reporting process of ADRs in Lagos state tertiary hospitals. It was aimed to evaluate the awareness and knowledge of ADR reporting among patients to determine the challenges they face while reporting. Therefore, the researcher used deductive survey questions to gain a better understanding of the issue and context involved in the study.

Two different questionnaires were administered to the groups to obtain applicable information from them. For HCPs, a goggle form which consisted of 21 questions was used for the questionnaire. While for the patients, a google form that consisted of 19 questions was used for the questionnaire. The questions were structured under 5 sections which facilitated the collection of the demographic data and opinions of the respondents respectively to fulfil the goal of the study. The categorical data method was used for the questions to ease subsequent data analysis upon the collection of information from the respondent. To strengthen the philosophy of the positivism approach, the survey was completed in the absence of the author, and all response gotten was a free expression of opinions without any risk of bias, influence, and interactions with the respondent.

The first part of the survey was a plain language statement that was designed to explain the aim of the study to the participants and gain their consent to use their answers exclusively for the research purpose only. Participants were assured that their participation was completely voluntary, and the privacy of every participant is highly assured as all responses will be fully anonymous and strictly confidential. They were also informed that all generated data will be stored in line with the General Data Protection Regulation (GDPR).

3.6. Data Collection

As detailed in the research strategy, the researcher collected her primary data through the use of a highly structured questionnaire which was designed for both patients and HCPs of Lagos state tertiary hospitals considered for the study. All questions were designed to tackle the relevant information needed to successfully ascertain the opinions of the HCPs and patients in the aforementioned study site to achieve the research aims and objectives.

According to Saunders et.al 2009, the best approach to achieve a great outcome of an exploratory study is to use a semi-structured or unstructured interview. Therefore, to support my quantitative findings, a semi-structured interview was used to help achieve exploration studies, the researcher used this method to facilitate further inquiry from the participants about their answer to get a better understanding of their answers and the impact/influence behind the answers given by asking them to further explain their answers. The respondents were asked a list of questions that slightly varied from interview to interview. The interview approach helped the researcher disclose areas previously not considered which helped contribute significantly to fulfilling her research objectives, achieve robust and very detailed data, and/or restructuring her approach or questions.

3.7. Sources of Data

Figure 7: Sources of data, created by the author

To fulfil research aims and objectives, the researcher used both primary and secondary data to gather information. The primary data was the main source of information and it consisted of 21 questions for HCPs and 19 questions for patients which were used to gather relevant data for her research. The researcher gathered information from 405 participants which included 135 HCPs and 270 patients.

The source of the research primary data included; contacts derived through professional alumni forum of teaching hospitals in Lagos, networking and LinkedIn contacts, referral from relatives that are healthcare professionals, referral from her family doctor, referrals from friends that are health professionals, and ex-colleagues and their referrals. Furthermore, sources of the secondary data includes- peer-reviewed journals and articles, accredited websites, databases, and academic write-ups.

3.8. Sampling Plan

This study sampling frame for the quantitative methodology consists of 405 participants which include 135 HCPs, and 270 patients from different tertiary hospitals in Lagos state Nigeria. A random sampling technique was employed to choose the participants to ascertain fair participation in the survey. While for the qualitative methodology, purposive and snowballing sampling techniques were deemed appropriated to select 6 highly experienced HCPs which include 2 doctors, 2 pharmacists, and 2 nurses in different tertiary hospitals in Lagos State. This sampling plan was chosen because it requires using a group of people who shows/experience a similar phenomenon of interest which in turn helps the researcher to get vital and reliable information needed to fulfil research purpose.

3.9. Access and Ethical

Accessibility of data is very crucial for the completion of a research and it is important for researchers to consider the extent and nature of access required to meet set objectives, and to also consider how they will gain sufficient access required to meet their objectives and complete their research. The researcher used her familiarity and understanding of the tertiary hospitals to gain access to her research data source, she used her existing contact of HCPs to get referrals to develop new contacts that helped contribute to her data source (Saunders *et al.*, 2009).

Before commencement of the interview, an audio-based briefing was given to each respondent to explain the purpose of the research and why she's researching that it is part of her academic requirement to fulfil her master's program, and highlight the possible benefit is of the research

to the hospital to ensure she gains sufficient access required to fulfil her research objective and completion. Furthermore, she clearly defines the type of access required and provided a brief introductory explanation of the research to the participants to enable them to have a clear insight of the study and to ensure their reply corresponds with the research objectives.

Concerning the ethics, the researcher ensures that all questions asked in the questionnaire and during the interview requested no personal information of the participants, and they were strictly related to the study and it is objective. It was clearly stated that the study was voluntary, and they can opt to withdraw or stop at any point they wish to. Furthermore, in compliance with Griffith College Dublin regulations and guidelines, the respondents informed consent was obtained before conducting the interview stating that their identity would be completely anonymous and a consensus was asked before audiotaping the interview. She ensured the interview was conducted professionally and ethically which did not subject her study group to any form of harm or embarrassment. After a complete agreement and understating of all the stated criteria and conditions, the interview was conducted and recorded simultaneously. The researcher treated all data obtained with optimum confidentiality and anonymity, and ensure they are not misinterpreted while transcribing it.

3.10. Techniques for Data Analysis

The quantitative data collected from the respondents were analysed using statistical methods because the data was quantifiable. Statistical Package for Social Sciences (SPSS) tool was used to analyse the results, and chi-square test was used as an appropriate descriptive statistic of frequencies and percentages to test relationships between categorical variables, assess the uniformity of data collected from the respondents, and to display the distribution of responses. The test was used to determine if there is a statistically significant difference between the expected and observed frequencies to test that the variables are independent in one or more categories.

For the qualitative data, the data obtained from the respondents were analysed through Deductive Thematic Analysis approach as the analysis technique to capture a rich and more in-depth data and provide a description and understanding of the answers obtained from respondents. Thematic analysis can be described as a method in which patterns and topics are defined, analysed, and interpreted. This method of data analysis proceeds through six models which include (I) Familiarization- transcribing the audio and reading through the transcribed text; (II) “Coding” of texts to highlight similar response pattern and important points from

respondents; (III) Generating themes through coded text; (IV) Reviewing of themes; (V) Defining and renaming of the themes; and (VI) Producing the report by writing up a theme to appropriately capture research observation and conclusions (Nowell *et al.*, 2017).

3.11. Conclusions

A research methodology is an integral part of research investigations, it highlighted specific tools and methodology employed by the researcher. For this research, a mixed-method approach that was underlined by a positivist philosophy was adopted. This approach led to quantitative and qualitative approached for data collection; an online survey, semi-structured phone interview, and the techniques used to analyse the data obtained were explained alongside how ethical concerns and their implications were handled. This ensured a better insight and perspective on the research study as well as obtaining measurable facts required for the analysis.

The data obtained were compared to the findings gathered during the literature review which was discussed in the previous chapter. The findings and analysis of data obtained from respondents will be discussed in the next chapter.

CHAPTER 4: RESEARCH FINDINGS AND ANALYSIS

4.1. OVERVIEW

This chapter presents the analysed results of answers generated from the survey questionnaire, a total of 405 responses were obtained and qualified for data analysis. The data generated assisted the author to determine the awareness, knowledge, and hindrances encountered by both HCPs and patients, as well as the opinions of HCPs towards direct patients reporting of ADRs. Descriptive statistics and percentages were used to present the data, and the data were analysed using google forms, SPSS, and chi-square tests.

4.2. ANALYSIS OF HCPs RESPONSES

Response Rate: The survey was administered to a total of 150 HCPs for 18 days (23rd July – 9th August). It consisted of 50 doctors, 50 pharmacists and 50 nurses, 135 accepted responses were received resulting in a response rate of 90%.

4.2.1. HCPs Demographics (Question 1 – 3)

Table 3: HCPs Demographics

		n	%
1. Which healthcare professional is completing this survey?	Doctor	38	28.1
	Nurse	29	21.5
	Pharmacist	54	40.0
	Pharmacologist	5	3.7
	Others	9	6.7
2. How long have you been practicing in this field?	Less than 1 year	15	11.1
	1 - 5 years	66	48.9
	6 - 10 years	31	23.0
	More than 10 years	23	17.0

Table 3 presents demographics of HCPs that responded to the study. It could be seen from the result that 28.1% of the respondents were doctors, 21.5% were nurses, 40.0% were pharmacists, 3.7% were Pharmacologists and 6.7% were in other specialist professional categories. The distribution of respondents based on their length of practice showed that 11.1% had practiced for less than a year, 48.9% had practiced for 1 – 5 years, 23.0% had practiced 6 – 10 years and 17.0% had practiced more than 10 years.

4.2.2. Level of Awareness/Knowledge about ADR

- **Question 3-5:**

Of all the respondents, 77.8% of the respondents are aware of ADR definition by considering it to be unexpected/serious reaction after taking a drug, while 14.8% considered it to be any reaction from drug therapy, 7.4% considered it to be expected and predicted reaction, establishing that have no basic knowledge of ADR definition.

On knowledge of organizations responsible for handling ADRs reports and pharmacovigilance in Nigeria, the distribution showed that 13.3% considered it to be the Federal Ministry of Health, 71.9% considered it to be NAFDAC, 8.9% considered it to be NCDC while 5.9% stated that they do not know.

The distribution of respondents' knowledge about whether the assessment and reporting of ADRs were incorporated into the orientation program curriculum of newly employed HCPs in their hospital showed that 48.9% considered that it was so, 34.8% considered that it was not so and 16.3% stated that they do not know.

Table 4: Knowledge about ADR

		N	%
3. What is your understanding of ADR (ADRs)?	Unexpected/Serious reaction after taking a drug	105	77.8
	Any reaction from a drug therapy	20	14.8
	Expected and predicted reaction	10	7.4
	Total	135	100.0
4. Which of the following organization is responsible for handling ADRs reports and Pharmacovigilance in Nigeria?	Federal Ministry of Health	18	13.3
	Nigerian Agency for Food and Drug Administration and Control (NAFDAC)	97	71.9
	Nigeria Centre for Disease Control (NCDC)	12	8.9
	I do not know	8	5.9
	Total	135	100.0
5. Is assessment and reporting of ADRs incorporated into the orientation program curriculum of newly employed HCPs in your hospital?	Yes	66	48.9
	No	47	34.8
	I do not know	22	16.3
	Total	135	100.0

It is an interesting fact that a good number of the HCPs are aware of ADR basic knowledge and correctly stated NAFDAC as the organization responsible for handling submitted ADR reports in Nigeria. However, only 48.9% stated that it is incorporated into their orientation curriculum at their hospital. This implies that although a significant number of the respondents are aware of ADR definition but they do not have it in their hospital program, therefore their level of knowledge is purely theoretical and personal.

- **Question 6-9:**

Table 5 shows distribution of awareness about ADR assessment among the respondents. It could be seen from the result that majority of HCPs (n = Yes) agreed that they are not aware of how causality of ADRs is performed in Nigeria (60.0%). Among those who expressed knowledge, 18.0% considered it to be a traditional routine in their hospital while 82.0% did not consider it to be so.

Also majority of HCPs were aware of the standard procedure for ADR assessment and reporting in their hospital (52.6%). However, there was an equivocal opinion on whether there was an adverse event and therapeutic committee in their hospital as 50.4% agreed that there was and 49.6% disagreed.

Table 5: Awareness about ADR Assessment

	No		Yes		Total	
	n	%	n	%	n	%
6. Are you aware of how causality assessment of ADRs is performed in Nigeria?	81	60.0	54	40.0	135	100.0
7. If yes, Is it a traditional routine in your hospital?	111	82.0	24	18.0	135	100.0
8. Are you aware of any standard procedure for ADR assessment and reporting in your hospital?	64	47.4	71	52.6	135	100.0
9. Is there adverse drug events & therapeutic committee in your hospital?	68	50.4	67	49.6	135	100.0

This shows that majority of HCPs have no prior knowledge about causality assessment of ADR even though there is a standard procedure for it in their hospital. This can be attributed to the fact that it is not a traditional routine in most of the tertiary hospitals as stated by the respondents, and there is no adverse drug events & therapeutic committee in the hospital to help evaluates clinical use of drugs and develop applicable policies for managing drug administration and use.

- **Question 10-13:**

Table 6 examines HCPs opinions on ADR reporting and their frequency on reporting it. The results showed that most of the respondents considered that ADR assessment and reporting should be mandatory (87.4%) while 12.8% opined that it should be voluntary. Majority of them have observed ADR cases in their practice (82.2%) and in response to how often they reported ADR cases, 37.8% stated that they always reported it, 14.4% often reported it, 20.7% sometimes report it, 23.4% rarely report it while 3.6% never report. Finally, in response to the basic principles of reporting ADR, the most identified principle was completeness of report (77.0%) followed by timeline of reporting ADRs (68.1%) and reliability of patient judgment (60.7%).

Table 6: Knowledge about ADR

		n	%
10. In your opinion, do you think ADR assessment and reporting should be either?	Mandatory	118	87.4
	Voluntary	17	12.6
	Total	135	100.0
11. Have you observed any ADR cases in your practice?	Yes	111	82.2
	No	24	17.8
	Total	135	100.0
12. If yes, how often do you report it?	Always	42	37.8
	Often	16	14.4
	Sometimes	23	20.7
	Rarely	26	23.4
	Never	4	3.6
	Total	111	100.0
13. basic principles of reporting ADR	Completeness of report	104	77.0
	Timeline of reporting ADRs	92	68.1
	Reliability of patient judgment	82	60.7
	I do not know	9	6.7
	Total	135	100.0

As established from the table, majority of HCPs opted that ADR assessment and reporting should be a mandatory obligation in Nigeria and they correctly identified most of the basic criteria for reporting ADR, which indicates that they are aware of the importance of reporting ADR. However, they stated they have observed ADR cases in their practice within the past 12 months but on the average they rarely report observed cases.

- **Question 14-15:**

As depicted from the answers on table 7, it could be seen that most of them stated that they were not aware of the SMS short-code for reporting ADR in Nigeria (85.9%); and they do not think they were sufficiently trained and knowledgeable about how to assess and report ADRs (62.2%).

Table 7: Knowledge about ADR reporting

	Yes		No		Total	
	n	%	n	%	n	%
14. Are you aware of the SMS short-code for reporting ADR in Nigeria?	19	14.1	116	85.9	135	100.0
15. Do you think you are sufficiently trained and knowledgeable about how to assess and report ADRs?	51	37.8	84	62.2	135	100.0

In all the respondents, majority of them established that they have not heard of the SMS short code, and they stated that they have no sufficient knowledge about how to assess and report ADRs because they are not viable trained on it.

4.2.3. HCPs Perceptions Towards Direct Patient Reporting of ADRs

- **Question 16-19:**

Table 8 presents HCPs opinions about patients reporting ADRs. The result showed that most of them were not aware that NPC in Nigeria allows patients to report ADRs directly (59.3%), most thought reports given by patients can be a good source of ADRs information (77.8%), most do not think that patients can write valid and quality ADR reports compared to HCPs (85.9%) and they do not encourage direct patient reporting of ADRs rather than through their HCPs (67.4%).

Table 8: HCPs Perception towards patient reporting ADRs

	Yes		No		Total	
	n	%	n	%	n	%
16. Are you aware that the National Pharmacovigilance Centre (NPC) in Nigeria allows patients to report ADRs directly?	55	40.7	80	59.3	135	100.0
17. In your opinion, do you think the reports given by patients can be a good source of ADR information?	105	77.8	30	22.2	135	100.0
18. Do you think patients can write valid and quality ADR reports compared to HCPs?	19	14.1	116	85.9	135	100.0

19. Do you encourage direct patient reporting of ADRs rather than through their HCPs?	44	32.6	91	67.4	135	100.0

As established from the result, HCPs are not aware that patients can report directly to NPC, however the respondents seem to think their report can be a good source of ADR information if they make a report. Sadly, they have an opposing opinion that patients can't generate a valid and quality report like HCPs, and there was a broad agreement that they should not be allowed to report directly to NPC rather the report should go through their physicians to ascertain the quality before submitting to NPC.

4.2.4. Challenges of Reporting ADRs in Lagos State Tertiary Hospitals

This section presents the challenges encountered by HCPs during their ADR practice in Lagos state tertiary hospitals. The researcher presented the participants several options to help ascertain their opinions on possible hindrances they are facing.

- **Question 20:**

Table 9: Hindrances to ADR Reporting

	n	%
Insufficient information provided by the patient	103	76.3
Lack of knowledge on ADRs reporting	87	64.4
Too busy and not enough time to prepare and send an ADR report	67	49.6
Rigorous or complex reporting process	60	44.4
Inaccessibility of ADR report form	57	42.2
The urge not to report an already established ADR	52	38.5
Fear of facing legal penalty	49	36.3
Level of clinical knowledge makes it difficult to diagnose an ADR	43	31.9
Others	2	1.5

Table 9 revealed the hindrances of ADR reporting encountered by HCPs in tertiary hospitals. Based on the responses, majority agreed that most common hindrances to ADR reporting are insufficient information provided by the patient (76.3%), and lack of knowledge on ADRs reporting (64.4%), while others included, too busy and not enough time to prepare and send an ADR report (49.6%), rigorous or complex reporting process (44.4%), inaccessibility of ADR report form (42.2%), the urge not to report an already established ADR (38.5%), fear of facing legal penalty (36.3%), level of clinical knowledge makes it difficult to diagnose an ADR (31.9%) and others which include insufficient staffs and too much workload (1.5%).

This depicts that there are several bottlenecks that hinders effective ADR practice in Nigeria.

4.2.5. Recommendations for Improvement

This section presents the proposed recommendation for the respondents to choose from by agreeing or disagreeing to the provided options.

- **Question 21:**

Table 10: Recommendations towards ADR reporting

	Strongly Disagree		Disagree		Neutral		Agree		Strongly Agree	
	n	%	n	%	n	%	n	%	n	%
Increase awareness about pharmacovigilance by conducting conference and continuous education programs	0	.0	1	.7	6	4.4	29	21.5	99	73.3
Current regulations should be reviewed to make ADRs reporting a professional obligation	0	.0	1	.7	12	8.9	36	26.7	86	63.7
NPC should provide feedback for every reported ADRs	0	.0	0	.0	7	5.2	42	31.1	86	63.7
Pharmacovigilance and ADRs module should be incorporated into medical/nursing school curriculum	1	.7	0	.0	12	8.9	36	26.7	86	63.7
Patients need more education and awareness on ADR reporting	0	.0	2	1.5	15	11.1	41	30.4	77	57.0
Initiatives to encourage more direct patient reporting	2	1.5	6	4.4	38	28.1	46	34.1	43	31.9
Introduction of technological solutions to assist HCPs to collate past medical history towards ADRs assessment	0	.0	0	.0	16	11.9	46	34.1	73	54.1

Table 10 presents the distribution of responses on recommendation towards ADR reporting among the respondents. Interestingly, an overwhelming majority of respondents agreed (strongly agree + agree) to most of the proposed recommendations, however giving initiatives to encourage direct patients reporting which stated 66.0% seems to be the lowest agreed recommendation.

94.8% respondents agreed to increase awareness about pharmacovigilance by conducting conference and continuous education programs. 90.4% respondents agreed that current regulations should be reviewed to make ADRs reporting a professional obligation.

NPC should provide feedback for every reported ADRs (94.8%), pharmacovigilance and ADRs module should be incorporated into medical/nursing school curriculum (90.4%), patients need more education and awareness on ADR reporting (87.4%), initiatives to encourage more direct patient reporting (66%), and that introduction of technological solutions to assist HCPs to collate past medical history towards ADRs assessment (88.2%).

This established that the proposed recommendation can help achieve a viable and sustainable pharmacovigilance practice when adequately put in place.

4.3. ANALYSIS OF PATIENTS' RESPONSES

Response Rate: The survey was administered to a total of 300 patients for 18 days (23rd July – 9th August). 270 accepted responses were received resulting in a response rate of 90%.

4.3.1. Patients Demographics (Question 1-4)

Table 11 presents patients' demographics who responded to the study. The result from the table showed that 47.8% of the patients were female and 52.2% were male. The age distribution of patients showed that 60.4% were predominantly young adults aged between 18 – 30 years, 25.6% were 31 – 40 years, 10.0% were 41 – 50 years, 3.3% were 51 – 60 years while 0.7% were 61 years and above. The distribution of respondents' highest level of education showed that 64.1% had postgraduate education, 29.6% had undergraduate education, and 6.3% had secondary education. Finally, the distribution of patients' occupation showed that 7.8% were academic professionals, 35.6% were corporate/office workers, 28.9% were self-employed, 22.2% were students and 5.6% were unemployed.

Table 11: Patients Demographics

		N	%
Gender	Female	129	47.8
	Male	141	52.2
	Total	270	100.0
Age	18 - 30 years	163	60.4
	31 - 40 years	69	25.6
	41 - 50 years	27	10.0
	51 - 60 years	9	3.3
	61 and above	2	.7
	Total	270	100.0
What is your highest level of education?	Postgraduate	173	64.1
	Undergraduate	80	29.6
	Secondary education	17	6.3
	Total	270	100.0
	Academic Professionals	21	7.8

Which of these categories do you belong to?	Corporate/Office Worker	96	35.6
	Self Employed	78	28.9
	Students	60	22.2
	Unemployed	15	5.6
	Total	270	100.0

4.3.2. Patients Level of Awareness/Knowledge

- **Question 5-9:**

This section presents the opinions and distribution of patients' response on reporting of ADRs. Of all the respondents, 63.3% have experienced ADR, 29.3% have not experienced it while 7.4% do not know. Among the respondents who have experienced an ADR, most action that patients had taken in response to the experienced ADR is stopped using the drugs (43.3%), while others include, informed a healthcare professional (36.3%), did nothing because the reaction was tolerable/stopped on it is own (17.0%), treated ADR with another drug (2.3%) or changed to a different drug type to continue original therapy (1.2%).

Majority of the patients stated that they knew how to report an adverse drug reaction when they notice one (73.3%). The people to whom they would report to included doctor/nurse (74.7%), pharmacist (15.2%), NPC (8.1%) or a relative (0.5%).

As for how they became aware of ADR, the distribution shows that their common sources of information are patient information leaflet from the drug (28.9%), followed closely by the internet (26.7%), and HCPs (26.3%). While 9.6% stated that they knew about ADR through relative/friend and television/radio (2.2%), whereas 6.3% stated that they do not know what adverse drug reaction was.

Table 12: Experience with ADR

		N	%
Have you ever experienced an adverse drug reaction?	Yes	171	63.3
	No	79	29.3
	I do not know	20	7.4
	Total	270	100.0
If yes, what action did you take when you experienced it?	Stopped using the drug(s)	74	43.3
	Informed a healthcare professional (doctors, nurses, pharmacists)	62	36.3
	Did nothing because the reaction was tolerable/stopped on it is own	29	17.0

	Treated ADR with another drug	4	2.3
	Changed to a different drug type to continue original therapy	2	1.2
	Total	171	100.0
Do you know how to report an adverse drug reaction when you notice one?	Yes	198	73.3
	No	72	26.7
	Total	270	100.0
If yes, to whom do you report the adverse drug reaction?	Doctor/Nurse	148	74.7
	Pharmacist	30	15.2
	National pharmacovigilance centre (NPC)	16	8.1
	Relative	1	.5
	Declined to indicate	3	1.5
	Total	198	100.0
Which of the following sources did you obtain information about ADR?	HCPs (doctors, nurses, pharmacist)	71	26.3
	Patient information leaflet from the drug	78	28.9
	Internet	72	26.7
	Relative/Friend	26	9.6
	Television/Radio	6	2.2
	I do not know what adverse drug reaction is	17	6.3
	Total	270	100.0

This established that majority of patients have a basic understanding of what ADR is, but they are not aware of reporting directly to NPC rather will report to their HCPs or stopped using the drug. This depicts lack of awareness on basic reporting methods available to patients within their reach.

- **Question 10-15:**

As a follow up question to question 10-15, this section is to ascertain patients experience in reporting ADRs. Table 13 shows the distribution of patients' opinions on the reporting of ADR. The majority of the patients (64.4%) stated that they had never reported an ADR while 35.6% stated that they had. Among those who had ever reported an ADR, when asked how easy was the reporting process ranging from 1 which represented very difficult to 5 which represented very easy, 5.0% stated that the process was 1, 16.0% considered that the process was 2, 32.0% indicated that it was 3, 21.8% stated that it was 4 and 25.2% stated that it was 5.

Most of the patients stated that they were not discouraged from making a report (75.0%) compared to 25.0% who stated they were discouraged. (43.9%) of the respondents got feedback concerning their report, 32.3% did not get feedback and 23.8% were not sure. Most of the patients never reported an adverse drug reaction (58.0%), while 25.7% had reported once, and

16.3% had twice or more. The majority of the patients established that they never reported ADR when they notice it (45.4), while 21.5% report immediately after noticing it, 18.0% reported within a week, 8.3% within the month, and 6.8% more than a month later.

Table 13: Patient Reporting ADR

		n	%
Have you ever reported an adverse drug reaction?	Yes	96	35.6
	No	174	64.4
	Total	270	100.0
If yes, how easy was the reporting process?	1	6	5.0
	2	19	16.0
	3	38	32.0
	4	26	21.8
	5	30	25.2
	Total	119	100.0
Were you at any point discouraged from making a report?	Yes	67	25.0
	No	203	75.0
	Total	270	100.0
Did you get feedback concerning your report?	Yes	72	43.9
	No	53	32.3
	Not Sure	39	23.8
	Total	164	100.0
How many times have you reported ADR?	Never	157	58.0
	Once	69	25.7
	Twice or more	44	16.3
	Total	270	100.0
How soon do you make the report after noticing ADR?	Never	123	45.4
	Immediately	58	21.5
	Within the week	49	18.0
	Within the month	22	8.3
	More than a month	18	6.8
	Total	270	100.0

This shows that majority of patients have never reported ADR, while some that has reported stated that they never got feedbacks regarding the reported ADR. This can be attributed to lack of knowledge and awareness on how to report ADR and the importance of reporting it, while lack of feedback will also discourage the ones that has reported earlier from making subsequent reports.

- **Question 16:**

Table 14: Level of awareness about reporting ADR

	Frequency	Percent
Low awareness (<= 2.00)	162	60.0
High awareness (3.00+)	108	40.0
Total	270	100.0

Table 14 presents a classification of the respondents' level of awareness based on their responses to questions on whether they have ever experienced an ADR, know how to report an ADR when they notice one, have ever reported an ADR, or whether they were aware of the SMS short code for reporting ADR. From a total obtainable score of 4 points, patients who scored 2 points and below were rated as having low level of awareness while those with 3 points and above were rated as having high awareness.

The result showed that most of the respondents (60.0%) had low awareness of ADR reporting whereas 40% had high level of awareness (Figure 7). Therefore, most patients do not know there is an SMS code that can be used to report any experience ADR directly to NPC. This established poor performance of the regulatory agency in publicising importance of reporting ADR and the basic reporting methods that can help patients report more at the comfort of their home while generating more ADR reports for the country to promote drug safety practice.

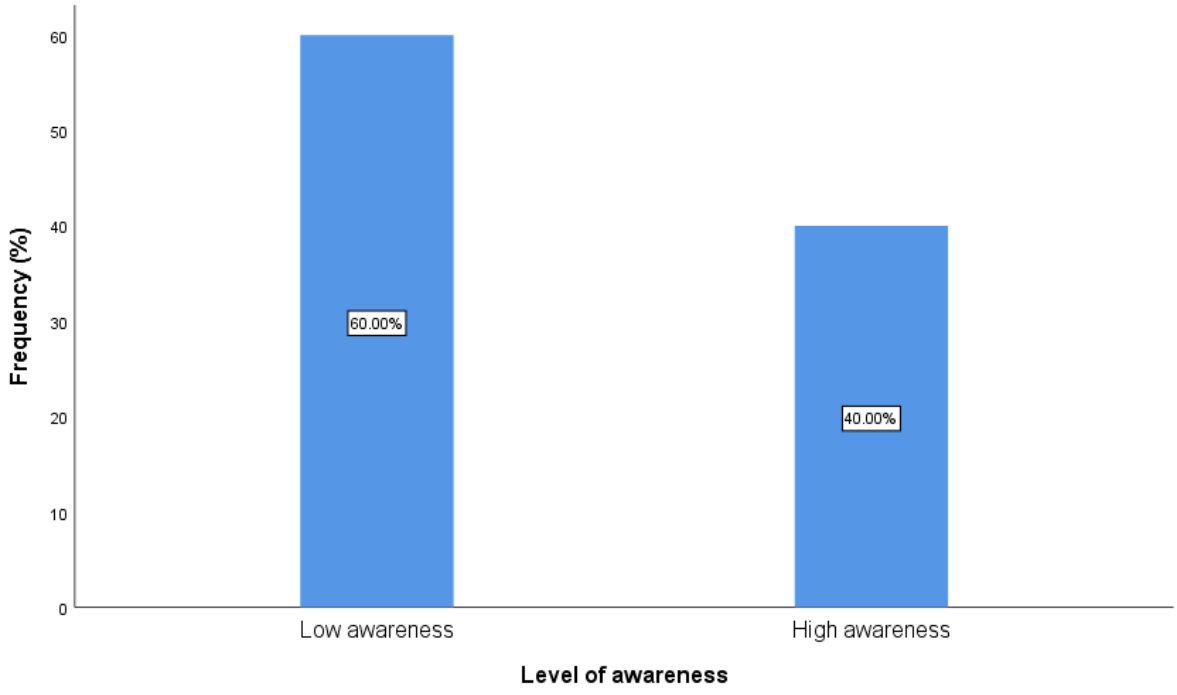


Figure 7: Level of patients' awareness

- **Question 17:**

- *Table 15: Reasons for not reporting ADR*

	Yes		No	
Reasons for not reporting ADR	n	%	n	%
Adverse reaction may not be serious	71	26.3	199	73.7
Adverse reaction resolved on it is own	51	18.9	219	81.1
Do not know how to report such reactions	147	54.4	123	45.6
Do not know the importance of reporting adverse drug reactions	133	49.3	137	50.7
Unsure if adverse drug reaction is related to the drug(s) used	108	40.0	162	60.0

Table 15 shows the reasons why patients chose not to report ADRs. Of all the respondents, an overwhelming majority stated they do not know how to report ADRs (54.4%), followed by respondents that stated they do not know the importance of reporting ADRs (49.3%), while being unsure if adverse drug reaction was related to the drug(s) used (40.0%). Other reasons included thinking that the adverse reaction may not be serious (26.3%) and having the adverse reaction resolving on it is own (18.9%).

The result depicts a broad response that indicates patients are not actively engaged and educated on the importance of reporting ADR.

4.3.3. Direct Patient Reporting Improvement

- **Question 18:**

Table 16: Preferred method for reporting ADR

	Frequency	Percent
Reporting directly to HCPs	169	62.6
Direct Phone call or text message to National Pharmacovigilance Centre (NPC)	61	22.6
Online, mobile/web application	29	10.7
Physically Filling a reporting form	10	3.7
Never reported before	1	.4
Total	270	100.0

Table 16 presents patients' preferred methods for reporting ADR. The findings showed that the most preferred method was to report directly to HCPs (62.6%). Other preferred methods included direct phone call or text message to National Pharmacovigilance Centre (NPC) (22.6%), online, mobile/web application (10.7%) and Physically Filling a reporting form (3.7%).

This depicts that irrespective of direct patient reporting to NPC, overwhelming majority of the patients still prefer to report to their HCPs rather than directly to NPC. This is because they believe they will get immediate feedback from their HCPs.

- **Question 19:**

This section presents the proposed recommendation for the respondents to choose from by agreeing or disagreeing to the provided options.

Table 17: Recommendation Towards Patient Reporting

	Strongly Disagree		Disagree		Neutral		Agree		Strongly Agree	
	n	%	n	%	n	%	n	%	n	%
Increase awareness about patients reporting ADRs through local news, social media, and NGOs	0	.0	3	1.1	10	3.7	41	15.2	216	80.0
NPC and HCPs should relate feedback to patients for every reported ADRs	0	.0	4	1.5	18	6.7	80	29.6	168	62.2
Reporting process should be made easier and more accessible	1	.4	1	.4	14	5.2	32	11.9	222	82.2

Table 17 shows the distribution of respondents on recommendation towards direct patient reporting of ADR. Interestingly, an overwhelming majority of respondents agreed (strongly agree + agree) to all the proposed recommendations.

95.2% agreed that there should be increased awareness about patients reporting ADRs through local news, social media, and NGOs.

91.8% agreed that NPC and HCPs should relate feedback to patients for every reported ADRs, and 94.1% agreed that reporting process should be made easier and more accessible.

This established that the proposed recommendation can help resolve underreporting issues, since patients can add value to pharmacovigilance structure by providing a more detailed reports with useful information which can help generate potential signals.

4.4. Test of Hypotheses

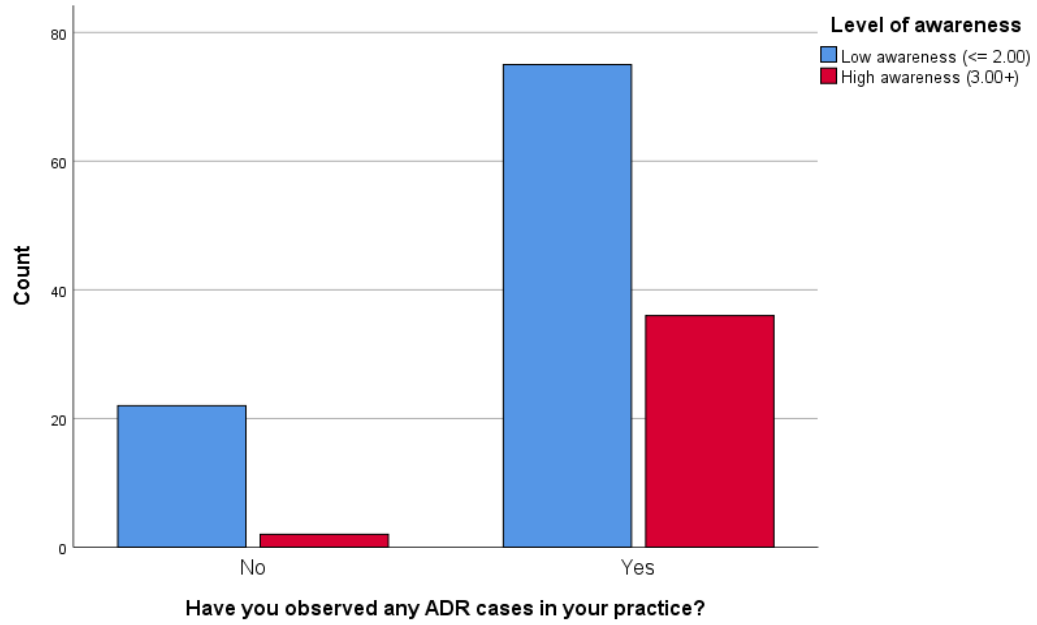
- **Hypothesis One:** There is no significant association between awareness on ADR and identification of ADR

The first hypothesis asked if there was no significant association between awareness on ADR and the identification of ADR in practice. This association was tested using Chi-square test of association at 0.05 level of significance.

Table 18: Chi-square test of association between level of awareness and observed case of ADR in practice

	Low awareness (<= 2.00)				High awareness (3.00+)				
	M	sd	n	%	M	sd	n	%	Statistics
No	.3	.65	22	91.7	4.0	.00	2	8.3	Chi-sq = 5.67
Yes	1.0	.82	75	67.6	3.8	.40	36	32.4	df = 1
Total	.8	.83	97	71.9	3.8	.39	38	28.1	p = 0.017

The result showed that there was a statistically significant association between the professionals' awareness of ADR and their observance of ADR cases in their practice (χ^2 = 5.67; $p < 0.05$), this implies that those who had high awareness tended to have high more number of cases observed. Based on the above, the H0 that there is no significant association between awareness on ADR and identification of ADR is rejected in favour of the H1 that there is a significant association between awareness on ADR and identification of ADR.



- **Hypothesis Two:** There is no significant association between patients' source of knowledge on ADR and their ability to identify and report any experienced ADR.

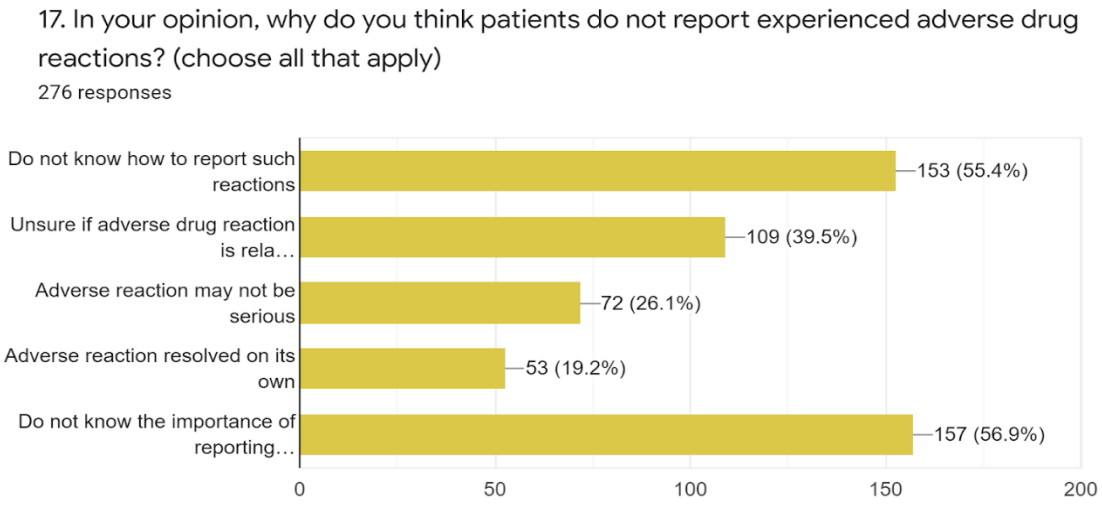
The second hypothesis asked if there was no significant association between patients' source of knowledge on ADR and their ability to identify and report experienced ADR. This association was tested using Chi-square test of association at 0.05 level of significance.

Table 19: Chi-square test of association between source of information about ADR and experience of ADR

Which of the following sources did you obtain information about ADR?	Have you ever experienced an adverse drug reaction?								Statistics
	I do not know		No		Yes		Total		
	n	%	n	%	n	%	n	%	
HCPs (doctors, nurses, pharmacist)	5	25.0	19	24.1	47	27.5	71	26.3	LR = 13.37
I do not know what adverse drug reaction is	5	25.0	8	10.1	4	2.3	17	6.3	df = 5
Internet	1	5.0	21	26.6	50	29.2	72	26.7	p = 0.02
Patient information leaflet from the drug	3	15.0	24	30.4	51	29.8	78	28.9	
Relative/Friend	6	30.0	5	6.3	15	8.8	26	9.6	
Television/Radio	0	.0	2	2.5	4	2.3	6	2.2	
Total	20	100.0	79	100.0	171	100.0	270	100.0	

LR = Likelihood ratio was used as the assumptions for the use of Chi-square test of association were violated.

The result showed that there was a statistically significant association between the source of information and experience of adverse drug reaction (LR = 13.37; $p < 0.05$), which implies that patients that are well aware and informed about ADR can easily identify when a reaction is side effect or ADR through their source of knowledge. Based on the above, we reject the H0 that there was no significant association between patients' source of knowledge on ADR and their ability to identify and report any experienced ADR in favour of the H1 that there is a significant association between patients' source of information about ADR and their ability to identify and report any experienced ADR.



Patients response on the ability of how to identify and report experienced ADR

- **Hypothesis Three:** Perception of HCPs has no impact on direct patient reporting of ADR in Lagos State Tertiary Hospitals.

The third hypothesis asked if Perception of HCPs has no impact on direct patient reporting of ADR in Lagos state tertiary hospitals. The association was tested using Chi-square test of association at 0.05 level of significance.

Table 20: Chi-square test of association between perception of HCPs and direct patient reporting of ADR in Lagos State tertiary hospitals

Do you think patients can write valid and quality ADR reports compared to HCPs?	Do you encourage direct patient reporting of ADRs rather than through their HCPs?						
	No		Yes		Total		Statistic
	n	%	n	%	n	%	
Yes	8	42.1	11	57.9	19	100.0	Chi-sq. = 6.44
No	83	71.6	33	28.4	116	100.0	df = 1
							p = 0.01

The result showed a significant association between perception of HCPs and it is impact on direct patient reporting of ADR in Lagos State tertiary hospitals (Chi-sq. = 7.35; $p < 0.05$). patients who were not discouraged from reporting tended to make more reports of ADR than those who were discouraged. Which implies that patients who seek the opinion of their HCPs before making a report directly will end up not using the direct patient reporting channel. Based on the above, the H0 that Perception of HCPs has no impact on direct patient reporting of ADR in Lagos state tertiary hospitals is rejected in favour of the H1 that Perception of HCPs has an impact on direct patient reporting of ADR in Lagos state tertiary hospitals.

4.5. Sociodemographic Factors and Level of Awareness

This section assesses the relationship between sociodemographic factors and level of awareness among the patients.

Table21: Test of association between sociodemographic factors and level of awareness

		Low awareness				High awareness				
		M	sd	n	%	M	sd	n	%	Statistics
1. Gender	Female	1.0	.82	73	45.1	3.1	.29	56	51.9	$\chi^2 = 1.20$

	Male	1.1	.82	89	54.9	3.1	.27	52	48.1	df = 1
	Total	1.0	.82	162	100.0	3.1	.28	108	100.0	p = 0.27
2. Age	18 - 30 years	1.0	.79	101	62.3	3.1	.30	62	57.4	LR = 6.06
	31 - 40 years	1.1	.87	43	26.5	3.0	.20	26	24.1	df = 4
	41 - 50 years	1.0	.85	15	9.3	3.0	.00	12	11.1	p = 0.20
	51 - 60 years	1.0	1.41	2	1.2	3.3	.49	7	6.5	
	61 and above	2.0	.	1	.6	3.0	.	1	.9	
	Total	1.0	.82	162	100.0	3.1	.28	108	100.0	
3. What is your highest level of education?	Postgraduate	1.1	.83	107	66.0	3.1	.29	66	61.1	$\chi^2 = 1.24$
	Secondary education	.5	.82	11	6.8	3.2	.41	6	5.6	df = 2
	Undergraduate	1.1	.77	44	27.2	3.1	.23	36	33.3	p = 0.54
	Total	1.0	.82	162	100.0	3.1	.28	108	100.0	
4. Which of these categories do you belong to?	Academic Professionals	1.0	.65	15	9.3	3.0	.00	6	5.6	$\chi^2 = 2.33$
	Corporate/Office Worker	1.2	.81	58	35.8	3.1	.23	38	35.2	df = 4
	Self Employed	1.0	.85	47	29.0	3.2	.37	31	28.7	p = 0.68
	Students	.9	.85	35	21.6	3.1	.28	25	23.1	
	Unemployed	1.4	.79	7	4.3	3.0	.00	8	7.4	
	Total	1.0	.82	162	100.0	3.1	.28	108	100.0	

The result showed that there was no significant association between the patients' level of awareness and their gender ($\chi^2 = 1.20$; $p > 0.05$); age ($\chi^2 = 6.06$; $p > 0.05$); highest level of education ($\chi^2 = 1.24$; $p > 0.05$); and their occupational category ($\chi^2 = 2.33$; $p > 0.05$). This implies that patients' characteristics (age, level of education and their occupational category) do not differ in their perception towards ADR, neither does it influence their decision to make a report or be more informed about ADR.

4.6. Qualitative ANALYSIS

4.6.1. Demographic Information

Respondent Characteristics	Sample size (n=6)
	Frequency
• **Gender**	
Male	2
Female	4
• **Experience Level (Years)**	
10	1
> 10	5
• **Role in the Hospital**	
Medical Doctor	2
Pharmacist	2
Nurse	2

4.6.2. Themes Formation

Phone Interview was conducted with 6 highly experienced HCPs from different tertiary hospitals in Lagos state Nigeria, to explore their perceptions on ADR assessment and reporting process, their perceptions about direct patient reporting, and also the challenges they face in the ADR practice. An abbreviated code was given to any class or theme recognized, and the purpose behind this is to connect topics in the obtained information and draw conclusions. Based on the respondents' similar qualitative opinions, five key themes were formed from the conducted interview and they will be discussed below alongside the response of the participants. The analysed result from the telephone interview with highly experienced HCPs helped to blend overlap with the survey questions and establish a meaningful conclusion and a better perspective of research goal.

4.6.3. Themes Discussion

The five identified key themes are discussed in this section and each of the thematic discussion contained some transcribed quotes from the participants which were used to support the theme discussion. The participants were numbered based on their role in the hospitals for instance, participants 1 and 2 are medical doctors, 3 and 4 are Pharmacists, while 5 and 6 are Nurses.

4.6.4. Theme 1 - Awareness/Knowledge on assessment and reporting of ADR

In the conducted interviews, this theme was constantly talked about and all the respondents demonstrated knowledge of pharmacovigilance and as well as the importance of ADR reporting. When respondents were asked to elaborate on their knowledge on ADR practice, convincing responses that solidified their awareness claim were obtained. They were all able to identify the regulatory body in charge of handling ADR reports, although only 50% of them correctly identified the location of the National pharmacovigilance centre operating in their geopolitical zone. When asked if they are *"aware of any form of casualty assessment of ADRs performed in Nigeria"?* 80% stated that they have not heard of it before while 20% established that they have personal knowledge about it and they know a few of the algorithms used to perform ADR assessment.

Furthermore, when asked if they *"perform ADR assessment before reporting it and how is the assessment performed to identify if reaction is an ADR"?* They were all able to demonstrate a great level of understanding on the importance of assessing ADR before reporting it. They all perform an assessment when a patient reports a reaction to them before concluding if it is an ADR or not. All the respondent described a common routine for assessing ADR when patients report to them; 80% go through patients' history to know if they have underlining health issues that can trigger effects, ask several questions to know if the patients followed advised drug usage routine and use patients' judgements and complain to decide, while 20% perform examination on patients and ask several questions to ascertain it is an ADR. Below are some of the response in the succeeding quote;

Participant 2 (17 years' experience) – *"Although my hospital presently does not have any standard procedure/mechanism for such practice. However, I personally go through the drug leaflet to ensure the patient complains is not one of the stated side effects of the drugs, and if it is not, I do some examination, some cases take pictures if patients do not mind, and ask them questions so I can make a formal ADR report using the yellow form".*

4.6.5. Theme 2 - Familiarity with ADR reporting methods

All interviewed participants demonstrated familiarity with the usage of ADR forms/ yellow forms, unfortunately, they are all unaware of the electronic reporting form available on the NAFDAC website and the SMS code introduced by NPC despite their years of experience and practice. Furthermore, only 50% was aware of the operating NPC in their geographical zone, while other respondents established that they have no idea where it is suited nor know if the centre is active.

In response to the question *"what form of ADR reporting are you conversant with?"* A similar response was obtained from all the participants explaining they are only aware of ADR forms and it is not easily available in their various tertiary hospitals.

Participant 2 (17 years' experience) – *I'm only aware of the ADR form which I started using during my internship as a young doctor and I am still using it now, although it is not always accessible most times when we need it and I am guessing the e-reporting and SMS code is a modern thing and it has not been fully introduced to we HCPs…."*

The truthful opinion from all the respondents about their unawareness of the other 2 methods of reporting ADR indicated the situation may be peculiar to a significant number of HCPs in Nigeria. They do not have sufficient knowledge on the awareness of the other two methods and hence they don't make any report if the form is not available.

4.6.6. Theme 3 - Prevalence of ADR cases

The respondents were asked, *"How often do you observe ADR cases in your practice within the last 12 months"?* The respondent all established that they frequently observe ADR in their practice but they sometimes do not report some of the cases they observe because they are not serious, unusual, or life-threatening. It was deduced that medical doctors and nurses experience more ADR cases in their practice because patients experiencing ADR usually go to their doctors or nurses rather than going to the pharmacists in the hospital. The doctors and nurses observe an average of 18 ADRs over the last 12 months of practice while the pharmacists observe an average of 7 cases over the same period. The pharmacists highlighted that reverse is the case in non-hospital settings as some of their colleagues that work in pharmacies tend to experience more ADR cases because of how easy it is for patients to purchase drugs without a prescription in pharmacies and they even tend to offer them treatment to any lodge complain rather than advising them to go see a doctor.

Additionally, based on the question and the response of the participants, the researcher was propelled to come up with the following question *"Do you get feedback or updates concerning*

the previously reported cases"? 80% established that they never get any feedback or update concerning previously reported ADR cases, while 20% established they get feedbacks mostly from pharmaceutical companies though it might take a while.

4.6.7. Theme 4 - Views on patient reporting of ADR

When asked if they are "*aware that patients can report directly to NPC and what is their perception towards it?"*. 80% said they are not aware that patients are allowed to report directly to NPC until the commencement of this interview, while 20% are aware. All respondents stated that based on their "views on the patient reporting practice" they do not support the idea of patient reporting directly to NPC and held a strong view against the idea because they believe patients can't generate a valid and quality report like the HCPs. Therefore, they should not be allowed to report directly, rather their report should pass through the HCPs for screening before it is being sent to NPC.

Participants 3 (12 years' experience) – *"I don't know that patient can report directly but since there is a system in place for that, the report should pass through their HCPs before the regulatory bodies because patients will only be able to describe how they feel but they might not be able to write down the valuable parameters needed to complete an ADR reporting, also most of them might fill the report halfway due to lack of knowledge or their busy schedule".*

But when participants 2 and 3 were inquired about direct patients reporting and their perspective towards it, their responses provided a sound insight because they both are aware of the practice and they highlighted positive benefit is the practice has brought. But despite their positive view about direct patient reporting, they still believe patients can't generate a valid report like the HCPs therefore the reporting process should be channelled through their physicians.

However, 50% of the participants highlighted that some benefit can come out of patients reporting if they are properly educated and guided because they have unique experiences and perspective. "*having a channel that encourages patient reporting will help achieve spontaneous ADR reporting because it will reduce the burden on HCPs and a combination of both patients and HCPs report will help generate more complete ADR report in the country if it is properly documented".*

4.6.8. Theme 5 - Common Challenges and Suggestions for Improvement of ADR Practice

All the engaged respondents established that promoting effective assessment and reporting of ADR in Nigeria will be a difficult task because some common challenges and constraints occur in all Nigerian hospitals when it comes to ADR practice. When asked that "*as a specialist what do you think is hindering effective ADRs reporting and assessment in Nigeria Hospitals, especially among HCPs, and what recommendation can you give in improving this"?* They highlighted several bottlenecks including; lack of feedbacks from regulatory authorities, insufficient manpower, lack of awareness and knowledge on ADR practice, lack of expertise in the field, excess workload, insufficient staff and time, inaccessibility of ADR forms, cumbersome reporting process, and fear of been penalized for making a report.

The respondents suggested improvements that can help NPC achieve spontaneous ADR reporting such as; *more awareness, Training, seminars, and workshop should be introduced frequently to constantly educate and remind HCPs about ADRs practice in Nigeria. Feedbacks should be provided to inspire HCPs. Cumbersome of the reporting process should be minimized to the lowest level or removed totally if possible, availability and accessibility of reporting forms, Nigerian regulatory agency should actively engage patients to report more so we can generate more ADRs reports in the country.*

They demonstrated a strong attitude and intentions towards reducing mortality and morbidity caused by ADR to ensure patient safety and reduce it is economic burden. The respondents agreed with the proposed recommendations in the survey and they believe putting all the due actions in place can change the situation of ADR in Nigeria, although it might be challenging but it is possible if the right course of action is put in place and followed diligently.

The response of the participants triggered another question which is *"Do you think ADR assessment and reporting should be mandatory or voluntary"?* All the participants established that assessment and reporting of ADR should a mandatory obligation of all HCPs. They highlighted that if it is mandatory they will all be forced to generate more reports and follow up on their patients regarding their medications. Additionally, they established that ADR reporting practice should be the duty of all HCPs and caregivers and not assume that it is the duty of a group of HCPs like the physicians, or pharmacists.

4.7. Conclusion:

The finding and analysis presented above shows the level of awareness and knowledge of HCPs and patients on ADR practice in Lagos state tertiary hospitals. As discovered from this research there are several bottlenecks in Nigeria healthcare system that hinders effective practice of ADR assessment and reporting. HCPs clearly identified the basic steps needed to assess drug reactions, and the basic principles needed to make a report. The knowledge on establishing causal relationship between suspected drug and reaction is below average and this was because most of them have no prior knowledge about it nor is it a traditional routine in their hospitals. Additionally, their perception towards patient reporting indicated they have a negative believe about the success of patient's direct reporting of ADRs. HCPs believe that patients do not have sufficient knowledge required to generate quality and valid ADR report, therefore their reporting process is meant to be channelled through their healthcare providers to ascertain the report.

Performance of patients on reporting ADR can be attributed majorly to their insufficient knowledge and awareness on the importance of ADR, it was established that their level of education or age doesn't influences their decision to make a report. Therefore, the general public needs to be educated and actively engaged to strengthen their impacts.

It was established that for both group of participants, insufficient knowledge and awareness is a major drawback on achieving effective ADR practice in Nigeria especially on the available reporting methods and knowing what ADR is. Although the regulatory agency in Nigeria (NAFDAC) has set in place the ideal models needed for reporting, however their performance towards awareness and publicity of adverse drug reaction was rated poorly and this in turn is a huge barrier in promoting drug safety practice and pharmacovigilance system in Nigeria. Fortunately, despite all the challenges, the HCPs exhibited a positive attitude towards achieving spontaneous ADR reporting if the appropriate resources and training are put in place, and majority of them are willing to update their knowledge personally to help reduce mortality and morbidity rate associated with ADRs and to invariably contribute to the overall pharmacovigilance structure in place in Nigeria.

CHAPTER 5: CONCLUSION AND RECOMMENDATION

5.1. Answering The Four Main Research Questions

Question 1: What are the assessment and reporting methods used by HCPs to identify and report ADRs in Lagos State tertiary hospitals?

From the response obtained in the survey and interview conducted with highly experienced HCPs, it was established that majority of the respondent have an average knowledge of what ADR is, how to report it, and the appropriate channel to forward their report to. They demonstrated several methods they used to assess ADR before reporting it to the appropriate channel, and some of this methods include; patient examination, patients' judgement and complaints, thorough questioning regarding the suspected drug and any other medication they are taking, however no one mentioned visual analogue scale which is more reliable to assess an ADR. Additionally, 80% of the respondents are not aware of what causality assessment is and the methods used to perform. They established that it is not a traditional routine in their hospitals, and they have no knowledge about it, also it was stated that is no awareness nor training on such practice to educate them and bring it to their notice.

The responses obtained also established that out of the three basic ADR reporting methods available in Nigeria, the respondents are only familiar with ADR form/yellow form, this contribute significantly to the under reporting issues in the country because the respondents established that the form is not readily available and accessible and that impact their decision on making a report.

Based on study, it is evident that there is a gap in the awareness and publicity of promoting causality assessment and the basic ADR reporting methods in Nigeria. This gap can be significantly associated to underreporting issues faced by the country despite the structured system put in place by NPC. The respondents of this study highly recommended consistent awareness and efficient information dissemination channel to help bridge the gap associated with lack of awareness and publicity on the assessment and reporting methods available in the country.

Question 2: What are the perceptions of HCPs towards patient reporting ADRs in Lagos State tertiary hospitals?

As established from the survey response and interview conducted, majority of the HCPs strongly oppose direct patient reporting and demonstrated a negative attitude towards it. Although a few of them are of the opinion that patients should be encouraged to make reports

because they believe their report can be a good source of ADR information since they are the ones experiencing the reactions. Despite the negative and positive views obtained from the HCPs regarding patients reporting, they are all of the opinion that patients do not have sufficient knowledge required to generate quality and valid ADR report, therefore their reporting process should be channelled through their healthcare providers to ascertain the report before going to NPC. This perception portrayed by HCPs establish that a cultural shift needs to transpire foster the cooperation of HCPs with the patient to autonomously report ADRs. The analysis of their perception present a gap that needs to be filled to ensure that HCPs see the importance of direct patient reporting so they can actively promote and encourage their patients since a combination of both groups can help resolve underreporting issues and promote drug safety practice worldwide.

Question 3: What is the level of awareness and knowledge of ADR among patients in Lagos state tertiary hospitals?

The response obtained from patients' survey established that the level of awareness among patients as regards ADR and it is basic reporting methods is very poor. Majority of the respondents has no knowledge about what ADR is and they have never reported experienced ADR because they do not know the importance of reporting such reactions and even how to report it. Furthermore, it was observed in the study that age, level of education, and occupational category doesn't influence patients' decision on reporting ADR, therefore the general public needs to be enlightened using all available medium and right source to create awareness and actively engage them to strengthened their impact. The research respondents suggested NPC should create more awareness on ADR, especially the SMS code created for direct patient reporting, and educate them more on the importance of reporting ADRs in other to bridge the barrier created due to lack of knowledge and awareness. Additionally, HCPs needs to educate their patients on their medication and possible risk associated with it so they can make a report when it is necessary since patients are a vital stakeholder in achieving spontaneous ADR reporting and establishing a viable pharmacovigilance system.

Question 4: What are the challenges impacting ADR assessment and responsible for the slow involvement of tertiary hospitals in Lagos State?

The response obtained from research respondents established that there are several bottlenecks and challenges impacting efficient ADR assessment and reporting in the aforementioned hospitals. This include- Insufficient staff, lack of knowledge on the assessment methods, lack

of resources, lack of feedback, time constraints, and rigorous/complex process. HCPs in tertiary hospitals are overwhelmed with workload due to the cadre of treatment they provide and influx of patients that uses the hospitals. They do not have enough time to perform ADR assessment and update their knowledge on the available methods for causality assessment. Additionally, most of these hospitals do not have an adverse drug event & therapeutic committee, and effective pharmacovigilance unit to help perform assessment on reported ADR cases and develop policies to manage drug use and administration. All the observed challenges cannot be neglected because they bear a burden on Nigeria healthcare system and they are significantly associated with the slow involvement of tertiary hospitals in Pharmacovigilance practice.

5.2. Results from Primary and Secondary Data Comparison

According to research carried out by Avery et al in the UK concerning patients reporting, author established that patients are justified to report directly if they are educated on the process and more awareness is created. Also, a study by *Inacio et al*, suggested a public awareness program should be created for patients reporting. This awareness will enable patient have distinct reasons to report and denote an altruistic behaviour towards reporting. This recommendation aligns with the responses obtained from this research on direct patient reporting that there should be more awareness, and they should be actively engaged to report more because they have unique experiences and perspective that can provide a more detailed report with useful information which can help generate new potential signals and add value to pharmacovigilance structure.

The regulatory agencies role and responsibility can't be overemphasized on sensitising HCPs and the public as regards drug safety practices. A common theme generated from previous studies and this research is to encourage more awareness and dedicate adequate resources to improve ADR practice globally. The general factors such as lack of knowledge/awareness, insufficient resources, poor ADR recognition, cumbersome of reporting process etc. associated with underreporting in other countries remains the same to a great extent as observed from this study and other studies conducted in Nigeria.

Additionally, results obtained on perceptions of HCPs towards direct patient reporting aligned with the outcome of similar research conducted in Malaysia by *Alshakka et al*, and in UK by *Krska* which established that HCPs are pessimistic about the success of direct patient's reporting of ADRs. About 70% of HCPs respondents in this study are not aware that patients can report directly, while 98% believe that patients do not have sufficient knowledge regarding

their medicines and hazards, therefore they can't produce quality information on ADRs nor generate a valid report.

5.3. Research Contributions and Limitations

Majority of previously conducted research on ADR showed gaps in tertiary hospitals; most studies were majorly focused on ADR reporting and a group of HCPs in Nigeria hospitals, but this research compared the major stakeholders in achieving spontaneous ADR reporting. It focused on tertiary hospitals and involved ADR assessment with several HCPs (Doctors, Nurses, Pharmacists) and patients in one study. Furthermore, no study in Nigeria has explored and evaluated perceptions of HCPs towards direct patient reporting, and the level of knowledge/awareness of tertiary hospitals patients regarding ADR and available reporting methods for patients in Nigeria. Based on the response obtained from 411 participants which was generated from both survey questionnaires and phone interviews that cut across all categories of tertiary hospitals in Lagos state Nigeria, despite the limited time and the unforeseen pandemic situation in the country. The findings from this research will help encourage direct patient reporting, and go a long way to help contribute to patients' awareness and educate them on ADRs and the basic reporting methods available within their reach (especially the SMS short code) since most studies exclude them and rather focus on HCPs.

This research will also help ensure HCPs are aware of benefit of direct patient reporting and improve their ADR practice to help reduce ADR burden faced by the country. It will provide them with useful insights into causality assessment of ADR, and basic ADR reporting methods especially the SMS code which is established on the NPC website but it is unknown to both HCPs and patients.

The main limitation of the study was slow response from HCP participants for the survey, and accessibility to reach the interviewees due to their busy schedule as regarding the high number of covid-19 pandemic cases in the country. Some of the target participants called in advance to cancel the interview due to their busy schedule which led to a relatively small number of participants for the interview. Additionally, some of the participants proved hesitant to fully disclose their ADR practice and some level of accuracy to recall details, while some were also in a hurry to attend to patients which was reflected from the responses they provided in the transcripts. This led to interruptions during the interviews and the inability to deeply explore their perceptions as earlier planned by the researcher which could impact the interpretation of the result obtained. Finally, due to unforeseen pandemic and global lock down, the researcher could not get hold of submitted ADR reports to evaluate their completeness and perform

causality assessment on them to establish with certainty the potential causal relationship between drugs and ADR.

5.4. Recommendations for Practice

From research findings, it is evident that there is need to address lack of knowledge and awareness among HCPs as regards causality assessment of ADR and basic reporting methods available in the country. The regulatory agency needs to create more awareness and publicity on ADR practice in Nigeria, because despite the valuable resources available on their website, most of the respondents are still unaware of these basic resources or even utilised them.

Additionally, since the involvement of tertiary hospitals is still quite slow in implementation of most of the objectives stated in the pharmacovigilance policy. Active pharmacovigilance units should be positioned there to assess and monitor ADR cases regularly, especially causality assessment and make it a traditional routine in the hospital since most ADR evidence and cases arise from these settings due to high risk associated with their treatments. The bottlenecks and cumbersomeness of the process should be eliminated, feedbacks should be constantly provided to HCPs to encourage them to be actively involved in the assessment and reporting process, and strengthened pharmacovigilance practice in the country. Also the orientation programs of newly employed HCPs and undergraduate modules should include curriculum that focus on ADR assessment, importance and basic principles of reporting ADR, authorities in charge of handling ADR reports etc. while frequent training and seminars should be organised as well to update their knowledge on pharmacovigilance and drug safety practice.

HCPs need to adopt new parameters to proactively monitor and assess ADR continuously and integrates patient's safety as core value and practice, therefore they need to encourage and promote direct patients reporting by ensuring patients are aware of the risk their medications and a suitable course of action to take in case they occur. A culture of notification to enable smooth flow of information dissemination and promote patient safety needs to be deployed among HCPs.

Finally, NPC needs to establish a solid foundation to educate patients on the importance of reporting ADR and basic reporting methods available to them to help promote drug safety practice. The SMS code proved to be user-friendly but it is vital to address the issue of relating feedbacks to patients through that same channel to encourage them to use the feature more and be actively involved.

5.5. Recommendation for Future Research

Future research should be conducted on a larger group of participants and extended to tertiary hospitals in other parts of the country to explore in-depth perceptions. Future study should be conducted over a long period of time to carefully assess in-hospital incidence of ADRs to find out culprit medications, more information on drug exposure, and poor ADR recognition. Furthermore, this research only scratched the surface area of assessment and showed gaps in the knowledge of causality assessment performed in Nigeria. Future research should consider going deep into this topic and subject reported ADR cases into causality assessment to enable rapid detection of potential signals related to drug use, help identify rare and serious ADRs, and propose how the practice can be improved. Incompleteness of reports should also be assessed on submitted ADR reports to identify variances in quality of reported data, prevalence of ADR, and all other relevant missing data of submitted reported to NPC which hinders complete evaluation of submitted reports for drug causality.

Additionally, Future research should consider assessing ADRs related to herbal medicines which is broadly used by Nigerian population especially in the rural area of the country.

5.6. Conclusion and Reflection

The entire process of the research was rigorous, insightful and exciting. Findings from this research helped developed researcher's knowledge on ADR and gave her deeper insights into challenges faced by both HCPs and patients as regard ADR. The study also helped filling gaps on HCPs and patients' perspectives on ADR, and also gave answers to several questions the researcher wanted to understand especially perception of HCPs towards patient reporting as it is an area that has not been explored in Nigeria.

Nigeria is earmarked as a fast-developing country and a leading nation in the future, therefore the country has to be established on all aspect especially the healthcare system starting with it is HCPs and regulatory agency. However, from reviewed literature and findings obtained from the study, it can be deduced that global underreporting issues are significantly associated with lack of knowledge and adequate resources dedicated to identify, assess, monitor, and report potential ADRs effectively. The reporting and assessing medium in Nigeria tertiary hospitals is inadequately efficient and somehow being underutilized by Nigerians including it is HCPs and healthcare providers due to lack of dedicated resources to the process, and persistent focus on knowledge acquisition instead of it is implementation and feasibility. The resulting effect of this act is the burden of ADR faced by the country and inability to achieve required ADR

reported cases despite the high mortality and morbidity rate associated with ADR cases in the country.

Despite the several bottlenecks and loopholes which hinders ability to spontaneously report ADR and identify rare/serious ADRs that may occur after drugs are marketed. HCPs are willing to improve drug safety practices and pharmacovigilance system in Nigeria by acknowledging that ADR reporting law should be amended to a mandatory practice for all HCPs in order to incorporate sense of ownership, resolve underreporting issues, and variance in the quality of ADR report submitted.

It is essential that the Nigerian government, corporate bodies, citizens and all other stakeholders be aware of this collective goal and play their roles diligently towards achieving it. Patients should be educated, encouraged and actively involved on ADR reporting because they have the potential to add value to generated reports by providing a more detailed reports which can help detect likely causality and impact on patients' lives. Adequate resources and awareness should be dedicated to ADR practice, seminars, training and workshops should be frequently provided for HCPs in Nigeria. This will invariably contribute to overall pharmacovigilance structure and healthcare system in place in Nigeria.

References and Bibliography

Aagaard, L. *et al.* (2012) 'Global Patterns of Adverse Drug Reactions over a Decade: Analyses of Spontaneous Reports to VigiBase™'. *Drug Safety*, 35(12), pp. 1171–1182.

Adisa, R. and Omitogun, T.I. (2019) 'Awareness, Knowledge, Attitude and Practice of Adverse Drug Reaction Reporting among Health Workers and Patients in Selected Primary Healthcare Centres in Ibadan, Southwestern Nigeria'. *BMC Health Services Research*, 19(1), p. 926.

Akhideno, P. *et al.* (2019) 'Pattern of Medications Causing Adverse Drug Reactions and the Predisposing Risk Factors among Medical In-Patients in Clinical Practice: A Prospective Study'. *Journal of Medical Sciences*, 39.

Alshakka, M.A., Ibrahim, M.I.M. and Hassali, M.A.A. (2013) 'Do Health Professionals Have Positive Perception Towards Consumer Reporting of Adverse Drug Reactions?' *Journal of Clinical and Diagnostic Research: JCDR*, 7(10), pp. 2181–2185.

Avery, A.J. *et al.* (2011) 'Evaluation of Patient Reporting of Adverse Drug Reactions to the UK "Yellow Card Scheme": Literature Review, Descriptive and Qualitative Analyses, and Questionnaire Surveys'. *Health Technology Assessment (Winchester, England)*, 15(20), pp. 1–234, iii–iv.

Awodele, O. *et al.* (2018) 'Patterns of Adverse Drug Reaction Signals in NAFDAC Pharmacovigilance Activities from January to June 2015: Safety of Drug Use in Nigeria'. *Pharmacology Research & Perspectives*, 6(5).

Doherty, M.J. (2009) 'Algorithms for Assessing the Probability of an Adverse Drug Reaction'. *Respiratory Medicine CME*, 2(2), pp. 63–67.

Durrieu, G. *et al.* (2016) 'Completeness of Spontaneous Adverse Drug Reaction Reports Sent by General Practitioners to a Regional Pharmacovigilance Centre: A Descriptive Study'. *Drug Safety*, 39(12), pp. 1189–1195.

Edwards, I.R. and Aronson, J.K. (2000) *Adverse Drug Reactions: Definitions, Diagnosis, and Management*. *undefined*. Available at: /paper/Adverse-drug-reactions%3A-definitions%2C-diagnosis%2C-and-Edwards-Aronson/4bdaf5c03c6844cff848c5cba606f365a886fa14/figure/0

Federal Ministry of Health. (2012) *Nigerian-National-Pharmacovigilance-Policy-and-Implementation-February-2012-Abuja.Pdf*. Available at: https://www.who-umc.org/media/2800/nigerian-national-pharmacovigilance-policy-and-implementation-february-2012-abuja.pdf.

Gaurav Chhabra. (2017) 'Causality Assessment, Methods, Pharmacovigilance'.[Health & Medicine] Available at: https://www.slideshare.net/gauravchhabra399/causality-assessmentmethodspharmacovigilance.

Gor, A.P. and Desai, S.V. (2008) 'Adverse Drug Reactions (ADR) in the InPatients of Medicine Department of a Rural Tertiary Care Teaching Hospital and Influence of Pharmacovigilance in Reporting ADR'. *Indian Journal of Pharmacology*, 40(1), pp. 37–40.

Inácio, P., Cavaco, A. and Airaksinen, M. (2018) 'Current Trends in Pharmacovigilance: Value and Gaps of Patient Reporting'. *International Journal of Clinical Pharmacy*, 40(4), pp. 754–757.

Kaur, M. *et al.* (2019) 'A Pharmacovigilance Study of Adverse Drug Reactions in a Tertiary Care Hospital in Haryana'. *International Journal of Basic & Clinical Pharmacology*. DOI: 10.18203/2319-2003.ijbcp20194149.

Krska, J. (2013) 'Views of British Community Pharmacists on Direct Patient Reporting of Adverse Drug Reactions (ADRs)'. *Pharmacoepidemiology and Drug Safety*, 22(10), pp. 1130–1133.

Mckinsey. (2012) *McKinsey_Healthcare_Report_Strength_in_Unity.Pdf*. Available at: https://www.gs1.org/docs/healthcare/McKinsey_Healthcare_Report_Strength_in_Unity.pdf

McLernon, D.J. *et al.* (2010) 'Adverse Drug Reaction Reporting in the UK: A Retrospective Observational Comparison of Yellow Card Reports Submitted by Patients and Healthcare Professionals'. *Drug Safety*, 33(9), pp. 775–788.

Mishra, P. and Dhikav, V. (2016) 'Introduction to Pharmacovigilance'.

NAFDAC. (2017) *About NAFDAC – NAFDAC*. Available at: https://www.nafdac.gov.ng/about-nafdac/.

Noll, M. (2016) *An Introduction to Pharmacovigilance*. *The Scrutinizer*. Available at: https://thescrutinizer.org/an-introduction-to-pharmacovigilance/.

Nour, S. and Plourde, G. (2019) 'Pharmacovigilance'. In *Pharmacoepidemiology and Pharmacovigilance*. Elsevier, pp. 7–23.

Nowell, L.S. *et al.* (2017) 'Thematic Analysis: Striving to Meet the Trustworthiness Criteria'. *International Journal of Qualitative Methods*, 16(1), p. 1609406917733847.

Olowofela, A. (2018) 'Evaluation of Pharmacovigilance System Performance in South- South Nigeria'. p. 195.

Olowofela, A., Fourrier-Réglat, A. and Isah, A.O. (2016) 'Pharmacovigilance in Nigeria: An Overview'. *Pharmaceutical Medicine*, 30(2), pp. 87–94.

Opadeyi, A.O., Fourrier-Réglat, A. and Isah, A.O. (2018) 'Assessment of the State of Pharmacovigilance in the South-South Zone of Nigeria Using WHO Pharmacovigilance Indicators'. *BMC Pharmacology and Toxicology*, 19(1), p. 27.

Oreagba, I.A., Ogunleye, O.J. and Olayemi, S.O. (2011) 'The Knowledge, Perceptions and Practice of Pharmacovigilance amongst Community Pharmacists in Lagos State, South West Nigeria'. *Pharmacoepidemiology and Drug Safety*, 20(1), pp. 30–35.

Palleria, C. *et al.* (2013) 'Limitations and Obstacles of the Spontaneous Adverse Drugs Reactions Reporting: Two "Challenging" Case Reports'. *Journal of Pharmacology & Pharmacotherapeutics*, 4(Suppl1), pp. S66–S72.

Pierre-Louis Lezotre MS. (2014) *Pharmaceuticals Regulation - an Overview | ScienceDirect Topics*. Available at: https://www.sciencedirect.com/topics/medicine-and-dentistry/pharmaceuticals-regulation.

Population Stat. (2020a) *Lagos, Nigeria Population (2020) - Population Stat*. Available at: https://populationstat.com/nigeria/lagos.

Population Stat. (2020b) *Nigeria Population (2020) - Population Stat*. Available at: https://populationstat.com/nigeria/.

Satyen, P. (2013) *Clinical Causality Assessment for Adverse Drug Reactions - ProQuest*. Available at: https://search.proquest.com/openview/cc3979cc43c20323d1ea87a14a6efbb7/1?pq-origsite=gscholar&cbl=226517).

Saunders, M., Lewis, P. and Thornhill, A. (2009) *Research Methods for Business Students 5th Edition 2009 (Mark N.K. Saunders, Adrian Thornhill, Philip Lewis)*. Available at: https://www.academia.edu/40208075/Research_methods_for_business_students_5th_edition_2009_Mark_N.K._Saunders_Adrian_Thornhill_Philip_Lewis_.

Sengar, G. and Tripathy, P. (2011) *Pharmaceutical Regulatory Agencies and Organizations around the World: Scope and Challenges in Drug Development | PharmaTutor*. Available at: https://www.pharmatutor.org/articles/pharmaceutical-regulatory-agencies-and-organizations-around-world-scope-challenges-in-drug-development.

Shamna, M. *et al.* (2014) 'A Prospective Study on Adverse Drug Reactions of Antibiotics in a Tertiary Care Hospital'. *Saudi Pharmaceutical Journal*, 22(4), pp. 303–308.

Shewale, B. *et al.* (2009) 'Adverse Drug Reporting: Role of Health Care Professionals'. *Journal of Pharmacy Research*.

Sriram, S. *et al.* (2011) 'Prevalence of Adverse Drug Reactions at a Private Tertiary Care Hospital in South India'. *Journal of Research in Medical Sciences : The Official Journal of Isfahan University of Medical Sciences*, 16(1), pp. 16–25.

St.Luke's. (2020) *Cancer Clinical Trials - Cancer Care | St. Luke's Cancer Centre*. Available at: https://www.slhn.org/cancer/clinical-trials.

Varallo, F.R. *et al.* (2017) 'Imputation of Adverse Drug Reactions: Causality Assessment in Hospitals'. *PLOS ONE*, 12(2), p. e0171470. DOI: 10.1371/journal.pone.0171470.

WHO. (2019) *Safety of Medicines - A Guide to Detecting and Reporting Adverse Drug Reactions - Why Health Professionals Need to Take Action: Glossary*. Available at: https://apps.who.int/medicinedocs/en/d/Jh2992e/2.html.

WHO. (2020) *WHO | Pharmacovigilance*. *WHO*. Available at: http://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/en/.

World Bank Group. (2020) *World Bank Country and Lending Groups – World Bank Data Help Desk*. Available at: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519.

Worldometer. (2020) *Nigeria Population (2020) - Worldometer*. Available at: https://www.worldometers.info/world-population/nigeria-population/.

Yadav, S. (2008) 'Status of Adverse Drug Reaction Monitoring and Pharmacovigilance in Selected Countries'. *Indian Journal of Pharmacology*, 40(Suppl1), pp. S4–S9.

Yartsev, A. (2019) *Classification of Adverse Drug Reactions | Deranged Physiology*. Available at: https://derangedphysiology.com/main/cicm-primary-exam/required-reading/variability-drug-response/Chapter%20320/classification-adverse-drug-reactions.

APPENDIX

Section 1 of 6

Assessment and Reporting of Adverse Drug Reactions (ADRs) in Nigeria Tertiary Hospitals: Healthcare Professionals (HCPs) Survey

Dear Participant,

I trust you are doing well.

This survey is being used as part of my dissertation research to fulfill the requirements for the degree of Masters (MSc) in Pharmaceutical Business and Technology at Griffith College Dublin.

The purpose of this research is to understand adverse drug reactions assessment and reporting processes in tertiary hospitals in Nigeria and elicit healthcare professional's views and perceptions towards patients reporting adverse drug reactions in order to improve pharmacovigilance structure in Nigeria.

Participation in this research is completely voluntary, and the privacy of every participant is highly assured as all responses will be fully anonymous and strictly confidential. All data generated from this survey will be exclusively used for my research purpose only and they will be stored in line with the General Data Protection Regulation (GDPR).

The survey consists of 5 sections aimed at collecting information on participant's demographics, awareness, perceptions, challenges, and recommendations for improvement of Pharmacovigilance structure and ADR reporting in Nigeria.

This survey will take no longer than 7 minutes to complete, and by completing this survey, you are giving your consent for the use of the information you provide to be used for the purpose of this study.

Thank you for your participation, your responses are highly valued.

I have read and understood the above information, and I agree to participate in this research. *

- ○ Yes
- ○ No

After section 1 Go to section 2 (Section A)

Section 2 of 6

Section A

DEMOGRAPHICS

1. Which healthcare professional is completing this survey? *

- Doctor
- Nurse
- Pharmacist
- Other...

2. How long have you been practicing in this field? *

- Less than 1 year
- 1 - 5 years
- 6 - 10 years
- More than 10 years

After section 2 Continue to next section

Section 3 of 6

Section B

LEVEL OF AWARENESS/KNOWLEDGE

3. What is your understanding of adverse drug reactions (ADRs)? *

- ( ) Any reaction from a drug therapy
- ( ) Unexpected/Serious reaction after taking a drug
- ( ) Expected and predicted reaction
- ( ) I do not know

4. Which of the following organization is responsible for handling ADRs reports and Pharmacovigilance in Nigeria? *

- ( ) Federal Ministry of Health
- ( ) Nigeria Centre for Disease Control (NCDC)
- ( ) Nigerian Agency for Food and Drug Administration and Control (NAFDAC)
- ( ) I do not know

5. Is assessment and reporting of ADRs incorporated into the orientation program curriculum of newly employed healthcare professionals in your hospital? *

- ( ) Yes
- ( ) No
- ( ) I do not know

6. Are you aware of how causality assessment of ADRs is performed in Nigeria? *

- ( ) Yes
- ( ) No

7. If yes, Is it a traditional routine in your hospital? *

- Yes
- No

8. Are you aware of any standard procedure for ADR assessment and reporting in your hospital? *

- Yes
- No

9. Is there adverse drug events & therapeutic committee in your hospital? *

- Yes
- No

10. In your opinion, do you think ADR assessment and reporting should be either? *

- Voluntary
- Mandatory

11. Have you observed any ADR cases in your practice? *

- Yes
- No

12. If yes, how often do you report it?

- Never
- Rarely
- Sometimes
- Often
- Always

13. In your opinion, which of the following are the basic principles of reporting ADR? (choose all that apply) *

- [ ] Completeness of report
- [ ] Reliability of patient judgement
- [ ] Timeline of reporting ADRs
- [ ] I do not know

14. Are you aware of the SMS shortcode for reporting ADR in *

- ( ) Yes
- ( ) No

15. Do you think you are sufficiently trained and knowledgeable about how to assess and report ADRs? *

- ( ) Yes
- ( ) No

After section 3 Continue to next section

Section 4 of 6

Section C

PERCEPTION TOWARDS PATIENT REPORTING ADRs

16. Are you aware that the National Pharmacovigilance Center (NPC) in Nigeria allows patients to report ADRs directly? *

- ○ Yes
- ○ No

17. In your opinion, do you think the reports given by patients can be a good source of ADRs information? *

- ○ Yes
- ○ No

18. Do you think patients can write valid and quality ADR reports compared to healthcare professionals? *

- ○ Yes
- ○ No

19. Do you encourage direct patient reporting of ADRs rather than through their healthcare professionals? *

- ○ Yes
- ○ No

After section 4 Continue to next section

Section 5 of 6

Section D

CHALLENGES OF REPORTING OF ADVERSE DRUG REACTIONS (ADRs)

20. Which of the following issues hinder effective reporting of ADRs in your hospital? (choose all that apply) *

- [ ] Insufficient information provided by the patient
- [ ] Fear of facing legal penalty
- [ ] Too busy and not enough time to prepare and send an ADR report
- [ ] Lack of knowledge on ADRs reporting
- [ ] Rigorous or complex reporting process
- [ ] Inaccessibility of ADR report form
- [ ] The urge not to report an already established ADR
- [ ] Level of clinical knowledge makes it difficult to diagnose an ADR
- [ ] Other...

Section 6 of 6

Section E

RECOMMENDATIONS FOR IMPROVEMENT

21. In your opinion, which of the following recommendation do you think will improve adverse drug reactions assessment and reporting in Nigeria? *

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagr...
A. Increase aw...	○	○	○	○	○
B. Current regul...	○	○	○	○	○
C. NPC should ...	○	○	○	○	○
D. Pharmacovig...	○	○	○	○	○
E. Patients nee...	○	○	○	○	○
F. Initiatives to ...	○	○	○	○	○
G. Introduction ...	○	○	○	○	○

Section 1 of 4

Reporting of Adverse Drug Reactions (ADRs) in Nigeria Tertiary Hospitals: Patients Survey

Dear Participant,

I trust you are doing well.

This survey is being used as part of my dissertation research to fulfill the requirements for the degree of Masters (MSc) in Pharmaceutical Business and Technology at Griffith College Dublin.

The purpose of this research is to elicit patient's views and experience on reporting of adverse drug reactions in order to improve pharmacovigilance structure in Nigeria.

Participation in this research is completely voluntary, and the privacy of every participant is highly assured as all responses will be fully anonymous and strictly confidential. All data generated from this survey will be exclusively used for my research purpose only and they will be stored in line with the General Data Protection Regulation (GDPR).

The survey consists of 3 sections aimed at collecting information on participant's demographics, awareness, experience, and recommendations for improvement of patient participation and reporting of adverse drug reactions in Nigeria.

This survey will take no longer than 7 minutes to complete, and by completing this survey, you are giving your consent for the use of the information you provide to be used for the purpose of this study.

Thank you for your participation, your responses are highly valued.

I have read and understood the above information, and I agree to participate in this research. *

- ○ Yes
- ○ No

After section 1 Continue to next section

Section 2 of 4

Section A

DEMOGRAPHICS

1. Gender *

- Male
- Female

2. Age *

- 18 - 30 years
- 31 - 40 years
- 41 - 50 years
- 51 - 60 years
- 61 and above

3. What is your highest level of education? *

- No formal education
- Secondary education
- Undergraduate
- Postgraduate

4. Which of these categories do you belong to? *

- Academic Professionals
- Self Employed
- Students
- Corporate/Office Worker
- Unemployed

After section 2 Continue to next section

Section 3 of 4

Section 3 of 4

Section B

and even cause hospitalization.

5. Have you ever experienced an adverse drug reaction? *

- Yes
- No
- I do not know

6. If yes, what action did you take when you experienced it?

- Informed a healthcare professional (doctors, nurses, pharmacists)
- Stopped using the drug(s)
- Changed to a different drug type to continue original therapy
- Treated ADR with another drug
- Switched to herbal drug/home remedy
- Did nothing because the reaction was tolerable/stopped on its own

7. Do you know how to report an adverse drug reaction when you notice one? *

- Yes
- No

8. If yes, to whom do you report the adverse drug reaction?

- Doctor/Nurse
- Pharmacist
- National pharmacovigilance centre (NPC)
- Other...

9. Which of the following sources did you obtain information about adverse drug reactions? *

- ○ Patient information leaflet from the drug
- ○ Healthcare professionals (doctors, nurses, pharmacist)
- ○ Relative/Friend
- ○ Internet
- ○ Television/Radio
- ○ I do not know what adverse drug reaction is

10. Have you ever reported an adverse drug reaction? *

- ○ Yes
- ○ No

11. If yes, how easy was the reporting process?

	1	2	3	4	5	
Very difficult	○	○	○	○	○	Very easy

12. Were you at any point discouraged from making a report? *

- ○ Yes
- ○ No

13. Did you get feedback concerning your report?

- ○ Yes
- ○ No
- ○ Not Sure

14. How many times have you reported adverse drug reactions? *

- ○ Never
- ○ Once
- ○ Twice or more

15. How soon do you make the report after noticing adverse drug reactions? *

- ○ Immediately
- ○ Within the week
- ○ Within the month
- ○ More than a month
- ○ Never

16. Are you aware of the SMS shortcode for reporting ADRs in Nigeria? *

- ○ Yes
- ○ No

17. In your opinion, why do you think patients do not report experienced adverse drug reactions? * (choose all that apply)

- ☐ Do not know how to report such reactions
- ☐ Unsure if adverse drug reaction is related to the drug(s) used
- ☐ Adverse reaction may not be serious
- ☐ Adverse reaction resolved on its own
- ☐ Do not know the importance of reporting adverse drug reactions

After section 3 Continue to next section ▾

Section 4 of 4

Section C

DIRECT PATIENT REPORTING IMPROVEMENT

18. Which is your preferred method of reporting adverse drug reactions? *

- Reporting directly to healthcare professionals
- Direct Phone call or text message to National Pharmacovigilance Centre (NPC)
- Online, mobile/web application
- Physically Filling a reporting form
- Other...

19. In your opinion, which of the following recommendation do you think will improve patients reporting adverse drug reactions in Nigeria? *

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagr...
A. Increase aw...					
B. NPC and HC...					
C. Reporting pr...					