AWARENESS AND KNOWLEDGE OF DOCTORS, PHARMACISTS AND NURSES ON ADVERSE DRUG REACTION REPORTING SYSTEMS IN NAMIBIA.

BY

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Submitted as the dissertation component in partial fulfilment for the degree of Master of Health Sciences in the school of Health Sciences, University of KwaZulu-Natal.

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PREFACE

This dissertation is presented in manuscript format. The findings of the study are presented in chapter 3, as a manuscript as required by the regulations of the University of KwaZulu-Natal. This manuscript will be submitted for publication in the *Journal of Pharmacy Practice.* The reference list is cited according to the instructions for authors as required by the *Journal of Pharmacy Practice.* A complete reference list is included at the end of every chapter and according to the reference style of the University of KwaZulu-Natal.

The dissertation consists of four chapters as follows:

- Chapter 1: provides an introduction to the study as well as the aims, objectives and a brief overview of the methodology.
- Chapter 2: provides the literature background to the study.
- Chapter 3: consists of the results, discussion and conclusion written in a manuscript format.
- Chapter 4: provides the general conclusions, recommendations, limitations and strengths of the study.

ABSTRACT

Objective

Reporting of adverse drug reactions (ADRs) in Namibian public health facilities is routinely done through safety yellow forms which are forwarded to the Therapeutics Information and Pharmacovigilance Centre (TIPC) for further assessment and possible interventions. This study investigated the awareness and knowledge of healthcare practitioners (HCPs) regarding the ADR reporting system in the country.

Methods

A cross-sectional study was conducted via a self-administered questionnaire at two state hospitals in Namibia; one located in the Khomas region and the other located in the Hardap region. The questionnaire was distributed to HCPs in current practice dealing directly with medication and it included a combination of open-ended, closed-ended and multiple-choice questions. Questionnaires were distributed in hard copy form during the period of 1 October 2019 up until 15 December 2019. Data was coded and transcribed into Microsoft® Excel® 2016 and analysed with SPSS® for IOS version 24.

Results

One-hundred and three completed questionnaires were received. Sixty-eight percent of the respondents were nurses, 24.3% were medical doctors and 7.8% were pharmacists. The majority of HCPs (73.8% and 56.3% respectively) were able to define the terms "adverse drug reaction" and "pharmacovigilance" correctly while only 41.7% correctly defined "spontaneous reporting". The majority of HCPs (60.2%) have identified an ADR in practice; however only 36.9% reported this following the approved process. Only 48.5% of HCPs were aware of the safety yellow form for ADRs and 63.1% of HCPs did not know where to obtain the form. Furthermore only 37.9% of HCPs knew the name of the drug regulatory authority in Namibia.

Conclusion

Awareness and knowledge of ADR reporting systems by HCPs in Namibia is insufficient. While HCPs deem it necessary to report ADRs, reporting is unacceptably low leading to

serious concerns regarding continuous monitoring of drug safety. Pharmacists showed better awareness compared to other HCPs and can, therefore, be best utilised as focal points in pharmacovigilance protraction. Mass awareness programs by the TIPC and other stakeholders need to be established to expand pharmacovigilance among HCPs.

Keywords: Adverse drug reaction, awareness/knowledge, reporting, healthcare professionals, pharmacovigilance and Namibia.

DECLARATION 1 - PLAGIARISM

I, Garnet Ndlovu, declare that:

1. The research reported in this thesis, except where otherwise indicated, is my original work.
2. The work described in this thesis has not previously been submitted to UKZN or other tertiary institutions for purposes of obtaining an academic qualification, whether by myself or any other party.
3. This thesis does not contain other persons' writing, unless specifically acknowledged as being sourced from other researchers. Where other written resources have been quoted, then:
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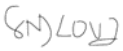
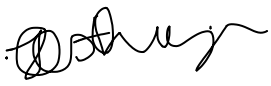
Signed  Date: 1 March 2020

This is to certify that the contents of this thesis are the original work of Mr Garnet Ndlovu and as the candidate's supervisor, I have approved this thesis for submission.

Signed: 

Name: **Dr Frasia Oosthuizen** Date: 15 March 2020

DECLARATION 2 – ETHICS APPROVAL

Ethical approval for the study was obtained from the Biomedical Research Ethics Review Committee of the University of KwaZulu-Natal (BE489/19) – (Annexure 1), as well as from the Ministry of Health and Social Services in Namibia (REF 17/3/3 GD) – (Annexure 2).

DECLARATION 3 – MANUSCRIPT PUBLICATION

1. My contribution to the project was as follows:

Garnet Ndlovu: Author – contributed to the project by performing all literature reviews, data and statistical analyses, interpretation of the results as well as manuscript preparation and writing of dissertation.

2. The contributions of others to the project were as follows:

Dr Frasia Oosthuizen*:* Supervisor – supervision of the concept of the study and writing of the dissertation and manuscript.

Dr Varsha Bangalee*:* Co-supervisor – supervision of writing of the dissertation and manuscript.

DEDICATION

I dedicate this thesis to my awesome family who have always supported me without wavering in all of my academic endeavours.

ACKNOWLEDGEMENTS

I would like to acknowledge my research supervisor, *Dr Frasia Oosthuizen,* for her continuous assistance, guidance, remarks and engagement before and throughout my thesis development.

I wish to sincerely thank the Ministry of Health and Social Services in Namibia for affording me the tremendous opportunity to conduct this research and the participants who were kind enough to set aside time from their hectic schedules to fill in the questionnaires.

To my daughter Reign, all of this is for you.

LIST OF ACRONYMS AND ABREVIATIONS

ADR	Adverse Drug Reaction
AIDS	Acquired Immunodeficiency Syndrome
HCP	Healthcare Professional
HIV	Human Immunodeficiency Virus
PV	Pharmacovigilance
NMRC	Namibia Medicines Regulatory Council
TIPC	Therapeutics Information and Pharmacovigilance centre
MOHSS	Ministry of Health and Social Services Namibia
MRSCA	Namibia Medicines and Related Substances Control Act
CPD	Continuing professional development
CEU	Continuing education units
HPCNA	Health Professions Council of Namibia
UKZN	University of KwaZulu-Natal
WHO	World Health Organisation

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CHAPTER 1

INTRODUCTION

"*Pharmacovigilance is concerned with two outcomes: safety and efficacy. Does a drug work and is it safe? It touches on almost every aspect of the drug lifecycle from pre-clinical development to post-market surveillance*" [Monique Ellis: 2017].

Adverse drug reaction (ADR) reporting is the cornerstone of drug safety in pharmacovigilance (PV) which involves the detection, evaluation and prevention of adverse drug effects [1]. Health professionals remain integral to the PV process to ensure that drug-related adverse events are appropriately identified, collected and subsequently reported to the relevant regulatory bodies.

ADR reporting relies on a system in place through which health professionals can delineate adverse drug effects to the relevant regulatory authorities. If there is no active awareness of such reporting systems, the level of ADR reporting remains remarkably low [1]. Being a cornerstone of PV, the question thus arises as to the knowledge of healthcare professionals (HCPs) with regards to ADR reporting procedures. The aim of this study is therefore to determine the level of awareness of ADR reporting processes in some facilities in Namibia as well as to determine if correct procedures are being followed to pass on the information as required by the drug safety regulatory authorities.

1.1 Background and rationale for this study

In all countries, national PV systems rely heavily on spontaneous reporting by HCPs, manufacturers or directly by patients. Of all the sources of data for drug safety monitoring, the spontaneous reporting by HCPs provides the highest volume of information at the lowest maintenance cost, and has proven its value in the early detection of safety issues related either to the products themselves or to their use [2]. The success of spontaneous reporting however requires substantial awareness and knowledge of such available systems from the HCPs concerned [2].

The lack of awareness and knowledge among healthcare professionals regarding ADR systems is very well-publicized in the literature [3, 4, 5]. This results in under-reporting and ADRs not always identified in preventable cases, especially in developing countries [6]. This lack of awareness has profound effects on the public health system as ADRs, which would normally

be detected, continue to contribute to high morbidity and mortality rates, putting an economic burden on already strained healthcare systems [7]. Levels of ADR reporting are universally poor and more effective dissemination and implementation of available knowledge is needed together with better use of the systems already available in place.

1.2 Research questions

This study focused on the following research questions posed to HCPs:

1.2.1 Do HCPs understand the term adverse drug reaction and have they ever encountered it in practice?

1.2.2 Is it necessary to report an ADR and do HCPs believe it is their professional obligation to do so?

1.2.3 What are HCPs' awareness of ADR reporting systems in Namibia?

1.2.4 Are HCPs aware of the existence of a Therapeutics Information and Pharmacovigilance centre (TIPC) at the Namibia Medicines Regulatory Council (NMRC) under the ministry of health and social services which handles ADR reporting?

1.2.5 What are HCPs' knowledge of the safety yellow forms for ADR reporting which are available at the facilities?

1.3 Aims and objectives of the study

The aim of this study was to assess awareness and knowledge of doctors, pharmacists and nurses (collectively referred to as healthcare professionals) in Namibia regarding ADR reporting procedures. To achieve this, the following objectives were outlined:

1.3.1 To determine if HCPs understand what ADRs are.

1.3.2 To determine if HCPs can detect ADRs.

1.3.3 To establish if HCPs deem it necessary to report ADRs as part of their professional responsibilities.

1.3.4 To establish if HCPs have the knowledge of processes that occur after submission of an ADR form.

1.4 Significance of the study

This study gives an indication of the extent to which HCPs in Namibia are aware of ADR reporting systems in the country with the aim to detect and minimize the occurrence of ADRs. Their knowledge of reporting systems was also determined to devise various educational interventions designed to influence reporting behaviour.

As per requirement by the Ministry of Health and Social Services in Namibia (MOHSS) as stated in the permission letter, the results of this study will be submitted to the Ministry upon completion. In particular, the Therapeutics Information and Pharmacovigilance Centre (TIPC) which falls under the NMRC will be able to use the results of this study to design robust intervention methods and awareness campaigns required to increase or improve ADR reporting awareness among nurses, doctors and pharmacists. It is envisaged that when HCPs are better equipped to detect and report ADRs through sensitization from the TIPC, there will be an increase in drug safety and positive patient outcomes. Accordingly, the TIPC will also be able to utilize the outcomes of this study to strengthen national pharmacovigilance systems as a mandate to the Namibian government in ensuring the national provision of medicines which are of good quality and are safe and effective.

Adverse drug reactions (ADRs) are a major cause of patient-related morbidity and mortality and awareness of HCPs to ADR reporting systems in Namibia will play a huge role in effective and safe clinical practice [8].

1.5 Research methodology

1.5.1 Study design and setting.

A cross-sectional quantitative survey, with the aid of a self-administered questionnaire, was conducted at two state hospitals located in the Khomas and Hardap regions in Namibia. The Khomas-based hospital is a referral-only, tertiary level, national institution which deals with larger patient volumes, while the Hardap-based facility is a district hospital that provides care at secondary level. The study targeted specific HCPs i.e. nurses, doctors and pharmacists. The survey was conducted from the 1st of October 2019 to the 15th of December 2019.

HCPs not included in this study were those who did not deal directly with medication and those who were not in practice at either of the two study sites. Awareness and knowledge of ADR reporting systems outside Namibia were also not considered.

1.5.2 Questionnaire design

All questionnaires were administered in English and consisted of 22 questions in total. The first four questions in section 1 of the survey assessed demographics such as type of profession, gender, educational qualifications attained and the number of years in practice. Section 2 included three open-ended questions that assessed knowledge of the terms "adverse drug reaction", "pharmacovigilance" and "spontaneous reporting". Section 3 of the questionnaire had fifteen questions and included a mix of both close-ended and multiple-choice questions designed to assess knowledge on specific ADR reporting systems in the country such as correct knowledge of the drug regulatory authority (question 20) and the ADR reporting tool (question 18 and 19). Section 3 also assessed knowledge on ADR causality (question 8), type of ADRs to be reported and for which products (question 9 and 10), the seriousness of ADRs (question 12), ADR identification, reporting and professional responsibility (question 11, 13, 14, 15 and 22), training on ADR reporting systems (question 16 and 17) and the actions that the regulatory authority can take after ADR form submission (question 21).

For the open-ended questions investigating knowledge of terms, the correct definition was determined by looking for key relevant wording in the responses and not necessarily the exact scientific definition. Some of the multiple-choice questions had more than one correct option to choose from and this was clearly indicated to the participants.

To improve the survey, the questionnaire was tested before use to determine if it was clear, relevant/appropriate to the study purpose and not open to more than one interpretation to eliminate any threat to face and content validity. To address this issue, a group of 10 HCPs (3 medical doctors, 5 nurses and 2 pharmacists) were piloted. All the HCPs involved in the questionnaire evaluation study were able to complete the questionnaire without any difficulty and their positive feedback to the simplicity and clarity of the questions was noted. These responses were not included in the data analysis.

1.5.3 Data Analysis

The collected data was coded, entered into Microsoft® Excel® 2016 and subsequently analysed using SPSS for IOS version 24. The data compiled was then analysed using descriptive statistics. Correlational techniques were further carried out to analyse the possible relationship between certain variables. ANOVA analysis was done to investigate if there were significant differences between the different professions in the way that they answered certain questions.

1.5.4 Ethical approval

Full ethical approval was obtained from the University of Kwazulu-Natal's Biomedical Research Ethics Review Committee (BREC) - reference number BE489/19. In line with BREC recommendations, distributed questionnaires were accompanied by a letter of invitation outlining the purpose of the study to the potential participants, as well as an informed consent document (see Annexure 5) which was signed by the participants.

1.5.5 Permission from Ministry of Health and Social services Namibia.

This study was given gatekeeper approval by the Ministry of Health Facilities. The research proposal was evaluated by the research department and found to have merit (REF number 17/3/3 GD).

1.6 Chapter 1 summary

This chapter summarizes the study's rationale and significance, research questions, aims, objectives and a brief outline of the research methodology.

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CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

The Namibia Medicines and Related Substances Control Act, (MRSCA) Act. No. 13 of 2003 requires every registration holder and healthcare professional to inform the Namibia Medicines Regulatory Council of any ADR which occurs during the use of any medicine [1]. Established in 2006 and officially launched in May 2008, the Therapeutic Information and Pharmacovigilance Centre (TIPC) was set up under the Ministry of Health and Social Services to promote the safe and rational use of medicines in Namibia. This has seen Namibia being fully admitted as the 90th member country and collaborating centre of the World Health Organisation (WHO) International Drug Monitoring program [1].

The specific objectives of the TIPC are to provide both proactive and query response information to HCPs and the general public in Namibia and to become a reference unit on pharmacovigilance by collecting and monitoring adverse reactions [1].

In developing nations such as Namibia, the scourge of infectious diseases such as malaria, tuberculosis and HIV has seen a fast track in the registration of essential medicines [1]. With prolonged use of these medications however, ADRs are more likely to be observed. The TIPC relies on information from HCPs on the ground by way of spontaneous reporting to monitor such adverse reactions. Spontaneous reporting of ADRs in Namibia is done via the completion of a "safety yellow form" (See Annexure 3) for onward submission to the NMRC.

Safety yellow forms are available in all public health facilities. HCPs can send the forms either directly to the NMRC, or the pharmacists in the hospitals who then forward the forms to the NMRC, which harbours the TIPC [1].

The information collected by the TIPC is entered into a database which is occasionally reviewed. This leads to one of many possible actions which can include labelling changes on the product, communication of alerts to HCPs about the adverse reaction and in some cases a complete withdrawal of the product from the market [1].

2.2 Previous recommendations on PV in Namibia

Adenuga (2018) highlights how ADRs are hugely under-reported by HCPs in Namibia [2]. The TIPC, however, as established by the MOHSS in Namibia, has not been fully utilised to its maximum potential since inception. About half of all nurses, doctors and pharmacists seem not to know how to report ADRs to the TIPC, let alone being aware of any ADR reporting systems in place [2]. This has led to recommendations which include the need for cross-sectional studies to be conducted in both the public and private sectors to investigate the awareness and knowledge of HCPs to ADR reporting systems in the country [2]. A further recommendation is that training on PV should also not be solely confined to the workplace, but also be incorporated into the academic curriculum to have a better chance of strengthening PV systems throughout the whole country [2].

2.3 PV monitoring and background.

The WHO programme for International Drug Monitoring first came into effect in the 1960s following the Thalidomide disaster [3]. Since then PV monitoring has grown exponentially, but mainly in developed countries, owing to reporting from healthcare professionals and pharmaceutical companies. In developed countries, ADR reporting systems and programs remain above par since early inception. For instance in the UK, 17000 ADR reports are recorded per annum according to the yellow card scheme [4]. In the US, active PV systems such as MedWatch and Sentinel Events Reporting Programs actively engage all HCPs [6]. The Netherlands has a large scale spontaneous ADR reporting program which was launched as early as 1963 [5]. A lot of resources are allocated into ensuring that HCPs are aware of these different ADR reporting systems [6]. Toolkits, such as SCOPE, have been widely introduced in European Union member states to increase awareness levels of national spontaneous ADR reporting systems [6]. Despite these major headways in PV advancement, adverse drug event reporting awareness in developed countries is still insufficient [7]. Studies that evaluated the knowledge and attitudes of US pharmacists regarding ADRs show that, despite favourable attitudes toward reporting, many pharmacists have never reported an adverse event or admit to having inadequate knowledge regarding reporting mechanisms [7]. This does not apply to the US alone, many other studies in several European countries have revealed a lack of pharmacist awareness with ADR reporting [5, 8, 10]. Pharmacists are regarded as the focal point of PV monitoring to ensure drug safety; however, if awareness to ADR reporting is scant among

pharmacists themselves, then this is more likely to be the same scenario for other HCPs such as doctors and nurses who are equally fundamental to PV propagation. A cross-sectional observational study by Gupta (2017) in India noted that 88% of doctors did not know the authority and the procedure for ADR reporting [16]. Shamim (2016) in southern India concluded that nurses had only moderate awareness and practice was very poor [9].

In low- and middle-income countries the situation remains perturbing: PV awareness, in general, remains a major challenge amidst strained resources and diversion of funds towards higher priority areas [7]. This places the majority of people at risk; developing countries have of late been getting an influx of new drugs either through direct importation or donations, unfortunately, some of these drugs may be of poor quality [15]. The drugs imported from developed countries may even have a different safety profile in some developing countries due to genetic and social differences [15]. In light of this, there is a dire need to strengthen ADR reporting systems in developing countries to minimize risks due to ADRs. All HCPs need to be omniscient to these systems as ADRs are preventable most of the time and awareness of early detection can be the difference between life and death. In the year 2011 in Pakistan, over 100 patients lost their lives because of counterfeit antihypertensive medication at a prominent cardiology hospital [9]. Needless to say, if HCPs at the time were aware of any PV system in place, this calamity would have been avoided on a larger scale.

2.4 Awareness and under-reporting.

Literature lists many barriers to ADR reporting and lack of awareness remains increasingly recurrent [9, 10, 11]. In fact lack of awareness is closely tied to under-reporting of ADRs and is very common [9]. It has been estimated that only 6-10% of all ADRs are reported [16]. In a cross-sectional observational study conducted in India, the main reason for the under-reporting of ADRs among resident doctors was due to a lack of awareness of the reporting procedure [16].

In another study conducted among nurses in both private and public hospitals in Dar Es Salaam, Tanzania, the majority (61.9%) of the participants strongly agreed that lack of knowledge about ADR reporting techniques contributed to fewer ADRs being officially registered to the regulatory authority [17].

2.5 Lack of awareness and knowledge of ADR reporting systems.

Lack of awareness of ADR reporting systems among HCPs has been highlighted in many research studies as the major impediment to successful PV [8, 9, 10, 16, 17]. In a 2017 study done in South Africa, a baseline analysis was conducted to investigate knowledge, attitudes and perceptions on adverse drug reaction reporting in a public sector hospital [10]. In this study, data was collected using self-administered questionnaires targeting all medical practitioners, nurses, pharmacists and pharmacist assistants at a public sector hospital. The vast majority indicated ADR reporting is necessary (96.2%) and that it is their professional obligation (89.4%), but only 18.9% were aware of an existing PV reporting system in the hospital, 15.2% had an ADR form available and 18.9% knew to whom the form should be submitted. Additionally, the vast majority had never reported an ADR. Owing to this dismal lack of awareness, the researchers had to recommend extensive training on ADR reporting.

In another study, awareness about ADR reporting among doctors, pharmacists and nurses was measured to determine reasons for ADR under-reporting in Pakistan public hospitals [9]. The findings depicted only 43.4% of HCPs knew the term pharmacovigilance and ADR reporting. Only 31.7% of respondents knew that there is an ADR reporting form at the website of the Drug Regulatory Authority of Pakistan (DRAP). Furthermore only 14.3% of HCP respondents knew that there is any ADR reporting organization in Pakistan. About 77.3% of respondents understood the importance of reporting ADRs although only 38.9% confessed the presence of ADR reporting systems in their respective healthcare system. Considering the importance of ADR reporting, the study showed inadequate knowledge among HCPs about adverse drug reactions and reporting.

A cross-sectional study was also done at selected public hospitals in northeast Ethiopia to investigate knowledge, attitude, and practice of 114 HCPs about ADRs [18]. One-hundred (87.7%) respondents knew that all drugs available in the market are not safe but only 23 (20.2%) respondents knew the term pharmacovigilance and understood its function. Likewise, 24 (21.1%) and 26 (22.8%) respondents knew about the availability of a national reporting system and ADR reporting form in Ethiopia, respectively. Thirty-five (30.7%) respondents knew the responsible body that monitors ADRs in Ethiopia. Moreover, a significant proportion of the respondents, 93 (81.6%) and 52 (45.6%) replied that ADRs should be reported only when they are serious and life-threatening and severe and cause disability, respectively. The study also found that only 24 (29.82%) respondents encountered at least one patient with ADR in the

past 12 months of their clinical practice, out of which 24 (70.59%) and 17 (50%) respondents recorded and reported ADRs, respectively. The study identified that HCPs had inadequate knowledge on ADR reporting and had poor ADR reporting practices which contributed to under-reporting in hospitals despite the majority having a favourable attitude towards ADR reporting. Taking into account the findings of the study, it was concluded that creating awareness and improving the knowledge of all HCPs through regular sensitization programs, trainings, and timely feedback is a very crucial strategy to enhance spontaneous ADR reporting in health facilities to the concerned body, which ultimately impacts the provision of quality patient care [18].

To emphasize the importance of awareness and sensitization, a Structured Pharmacovigilance and Training Initiative (SPHAR-TI) model based on the WHO accredited Structured Operational Research and Training Initiative (SOR-IT) model was designed to improve the reporting of ADRs in public health programs treating HIV, TB and Malaria in Nigeria [11]. The major finding of this evaluation was the significant gain in awareness and knowledge observed among the participants generally. Participants also developed the capacity to detect and accurately report ADRs, including serious ADRs such as Steven Johnson Syndrome and bilateral gynaecomastia.

This summarised literature review affirms the need to increase awareness of ADR reporting systems among healthcare professionals to improve public health and safety in relation to the use of medicines. Even in developed European countries with robust reporting and response systems, awareness still remains a major issue and there will always be a need to continually sensitize HCPs to the need for ADR reporting [7]. Priyadharsini (2017) appropriately sums it up in his study that HCPs were aware of the concept of ADRs but the majority did not know how and where to report. Thus, the creation of awareness amongst HCPs is the most important determinant influencing spontaneous reporting of ADRs. Safe to say, there will always be a need to address this awareness as long as ADRs are still one of the leading causes of morbidity and mortality in healthcare [12]. In Canada, ADRs cause 10000 to 22000 deaths and cost the Canadian healthcare system over $13 billion per year [12]. In the United States, 26500 children die from ADRs each year [12]. Unlike the pattern in high-income countries, the drugs implicated in ADR-related deaths in developing countries are mostly drugs used in the treatment of HIV and tuberculosis, reflecting the high burden of these diseases [15]. These ADRs are implicated in 2.5–18% of deaths of hospitalized patients and fatal ADRs are frequently preventable [13].

2.6 Other challenges to PV implementation.

Unfortunately, a few challenges affect the extent to which HCPs are aware of ADR reporting systems in their respective practices. Belete (2016) outlines how the unavailability of ADR reporting forms played a huge role in significantly discouraging healthcare professionals from detecting and reporting ADRs in Boru Meda Hospital, North East Ethiopia [14]. Awareness proves largely futile if the safety forms which are needed for reporting are not made readily accessible and this impacts poorly on achieving positive patient outcomes.

Regulatory authorities also have a mandate to ensure the establishment and maintenance of strong PV systems which are clear and concise enough to be followed by HCPs [14]. Healthcare professionals will not conform to any ADR reporting system which is ambiguous.

As much as HCPs are aware of ADR reporting systems available to them, other factors can also impede reporting such as difficulty in deciding if it is an adverse drug reaction or not, lack of motivation due to non-remuneration and a lack of time due to busy working hours or patient overload [9,10,11]. These issues are equally pertinent and also require equal priority.

2.7 Chapter summary

This chapter summarizes the literature review pertaining to the well-publicised lack of awareness of ADR reporting systems. It also highlights the background of PV in Namibia and the role of the TIPC in ADR reporting.

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CHAPTER 3

MANUSCRIPT FOR SUBMISSION AND PUBLICATION

3.1 Introduction

This chapter describes the general findings and discussion of the results of the study and is presented in the form of a manuscript entitled "Awareness and knowledge of doctors, pharmacists and nurses on ADR reporting systems in Namibia - a study in two state hospitals in the Khomas and Hardap regions".

3.2 Manuscript

Awareness and knowledge of healthcare practitioners on adverse drug reaction reporting systems in Namibia - a study in two state hospitals in the Khomas and Hardap regions.

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ABSTRACT

Objective

Reporting of adverse drug reactions (ADRs) in Namibian public health facilities is routinely done through safety yellow forms which are forwarded to the TIPC for further assessment and possible interventions. This study investigated the awareness and knowledge of healthcare practitioners (HCPs) regarding the ADR reporting system in the country.

Methods

A cross-sectional study was conducted via a self-administered questionnaire at two state hospitals in Namibia; one located in the Khomas region and another one located in the Hardap region. The questionnaire was distributed to HCPs in current practice dealing directly with medication and it included a combination of open-ended, closed-ended and multiple-choice questions. Questionnaires were distributed in hard copy form during the period of 1 October 2019 up until 15 December 2019. Data was coded and transcribed into Microsoft® Excel® 2016 and analysed with SPSS® for IOS version 24.

Results

One-hundred and three completed questionnaires were received. Sixty-eight percent of the respondents were nurses, 24.3% were medical doctors and 7.8% were pharmacists. The majority of HCPs (73.8% and 56.3% respectively) were able to define the terms "adverse drug reaction" and "pharmacovigilance" correctly while only 41.7% correctly defined "spontaneous reporting". The majority of HCPs (60.2%) have identified an ADR in practice; however only 36.9% reported this following the approved process. Only 48.5% of HCPs were aware of the safety yellow form for ADRs and 63.1% of HCPs did not know where to obtain the form. Furthermore only 37.9% of HCPs knew the name of the drug regulatory authority in Namibia.

Conclusion

Awareness and knowledge of ADR reporting systems by HCPs in Namibia is insufficient. While HCPs deem it necessary to report ADRs, reporting is unacceptably low leading to serious concerns regarding continuous monitoring of drug safety. Pharmacists showed better

awareness compared to other HCPs and can, therefore, be best utilised as focal points in pharmacovigilance protraction. Mass awareness programs by the TIPC and other stakeholders need to be established to expand pharmacovigilance among HCPs.

Keywords: Adverse drug reaction, awareness/knowledge, reporting, healthcare professionals, pharmacovigilance and Namibia.

Background and introduction

Namibia has an approximate population of 2.5 million and is classified as an upper-middle income developing country [1]. A high disease burden however exists and national public health disease control programmes, such as HIV/AIDS, malaria and tuberculosis programmes, have placed a large strain on the country's resources [1].These programmes have led to the extensive use of essential medicines and with this, the need for adequate safety monitoring. Adverse drug reactions (ADRs) that are not properly identified, reported and managed can cause harm and undermine the public's confidence in the health system [2]. The national guidelines for medicine safety surveillance underline spontaneous reporting by healthcare professionals (HCPs) to be effective enough for early detection of unknown problems and thus appropriate for the Namibian setting [3].

The Therapeutics Information and Pharmacovigilance Centre (TIPC) was established in 2006 with the purpose of providing therapeutics information, monitoring safety and ensuring rational use of medicines that are already on the Namibian market [3]. The safety yellow form, a simplified ADR reporting form that is made available at public health facilities in Namibia, is used to report any suspected ADRs for all conventional, biological, and complementary medicines, nutritional and dietary supplements and medical devices [3]. Completed safety yellow forms are submitted to the TIPC via fax or email where all case reports are analysed, summarised and sent to the clinical committee of the Namibia Medicines Regulatory Council (NMRC). After further exploration, the committee can recommend regulatory action which may include, but are not limited to, complete withdrawal of the product or sending out alerts to the prescribers, manufacturers and the consumers about the possible adverse reaction [3].

A well-documented challenge to the implementation of ADR reporting among HCPs is limited awareness and knowledge of existing reporting systems [4]. In a 2019 study, knowledge, attitudes and practices of HCPs towards ADR reporting in primary healthcare facilities in South Africa was investigated among 200 respondents [5]. Although an appropriate attitude towards ADR reporting existed, the actual frequency of ADR reporting was low (16.0%). Nearly two-thirds (60.5%) of respondents did not know how to report, where to report, or when to report an ADR. When results were combined, the overall mean score in terms of positive or preferred practices for ADR reporting was 24.6% with pharmacists having the highest scores. The study highlighted a void in ADR reporting awareness and knowledge which is widely prevalent in developing countries with a high disease burden like Namibia [1, 5].

The aim of this study was, therefore, to investigate the awareness and knowledge of HCPs in Namibia on ADR reporting systems in the country. Awareness and knowledge of these systems by HCPs forms the essence of medicine safety. Other factors having an influence on awareness and knowledge of ADR reporting systems in the country were also investigated among HCPs. These included knowledge on estimating the strength of a relationship between drug(s) exposure and the occurrence of ADRs known as causality assessment [3]. In line with the objectives of this study, knowledge on causality assessment will determine if HCPs can detect ADRs or not. Complimentary knowledge among HCPs on ADR severity, seriousness of ADRs and ADR reporting of certain products was also investigated as these have a cumulative effect on the intent of the study.

Methods

Study sample

The cross-sectional study was carried out with the use of a self-administered questionnaire which was completed by doctors, pharmacists and nurses at 2 state hospitals. The hospital situated in the Khomas region is the main hospital hub of the country and also deals with external referrals from smaller towns. In terms of staffing, it has approximately 30 doctors, 7 pharmacists and about 200 nurses. The state hospital in the Hardap region, which is the southern part of the country, handles smaller patient volumes. Only 2 pharmacists, 5 doctors and 29 nurses are stationed there.

One-hundred and twenty-three self-administered questionnaires were distributed between the two facilities as hard copies. The inclusion criteria consisted of HCPs (doctors, pharmacists and nurses) in full-time permanent employment at the two state hospitals dealing directly with medication. The exclusion criteria comprised of HCPs who do not deal directly with medication and those not in full-time practice at the two hospitals of interest.

Permission to conduct the study was obtained from the Ministry of Health and Social Services in Namibia (MOHSS) and ethical approval was acquired from the University of Kwazulu-Natal's Biomedical Research Ethics Review Committee (BREC); approval number BE489/19.

Sampling, data collection, ethical issues and analysis

In this study, two types of purposive sampling techniques were used - total population sampling and random sampling. Due to the small number of HCPs at the Hardap region hospital, all of the 36 HCPs were included in the study sample. All the doctors and pharmacists (n=37) at the Khomas central hospital were also sampled to take part in the study, but random sampling was initiated for nurses as the entire population of about 200 nurses was too big. A smaller sample size of 50 nurses were randomly selected from the medical adult ward, maternity/paediatric ward, oncology ward, psychiatry ward, HIV ward/clinic, and emergency ward. At a 95% confidence level with a margin error between 4 and 8%, 123 HCPs from a research population of approximately 273 was the ideal sample size.

Questionnaires were made available at the department heads' desks and the weekly department meetings. Effort was made to attend at least one of these meetings to address any questions that they might have had about the study. Willing participants were also asked to refer eligible friends or colleagues to take part in the study.

All questionnaires were administered in English and consisted of 22 questions in total. The first four questions in section 1 (question 1-4) of the survey assessed demographics such as type of profession, gender, educational qualifications attained and the number of years in practice. Section 2 (question 5-7) included three open-ended questions that assessed knowledge of the terms "adverse drug reaction", "pharmacovigilance" and "spontaneous reporting". For the purpose of this study, the term "pharmacovigilance" was defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem [8]. "Adverse drug reaction" was defined as a response to a medicine which is noxious and unintended, and which occurs at therapeutic doses and the term "spontaneous reporting" was defined as a system whereby case reports of adverse drug events are voluntarily submitted by health professionals and pharmaceutical companies to the national pharmacovigilance centre [8]. For the open-ended questions investigating knowledge of terms, the correct definitions were determined by looking for relevant key wording in the responses and not necessarily the exact scientific definition.

Section 3 (question 8-22) of the questionnaire had fifteen questions and included a mix of both close-ended and multiple-choice questions. Some of the multiple-choice questions had more than one correct option to choose from and this was clearly indicated to the participants. Under section 3; questions 8, 9, 10, 11 and 12 assessed knowledge on reporting, identification and

consequences of ADRs. Questions 13, 14 and 15 assessed if HCPs had ever identified or reported an ADR before in practice and if they thought it was their professional responsibility to do so. Training on ADR reporting was ascertained using questions 16 and 17 and the last five questions (18, 19, 20, 21 and 22) looked at awareness and knowledge of specific ADR reporting systems in Namibia. Question 21 specifically addresses the objective assessing if HCPs are aware of the processes which occur after submission of the ADR reporting form.

To improve the survey, the questionnaire was piloted before use to determine if it was clear, relevant/appropriate to the study purpose and not open to more than one interpretation to eliminate any threat to face and content validity. The questionnaire was piloted amongst a group of 10 HCPs (3 medical doctors, 5 nurses and 2 pharmacists). All the HCPs involved in the pilot study were able to complete the questionnaire without any difficulty and their positive feedback to the simplicity and clarity of the questions was noted.

Distributed questionnaires were accompanied by an information sheet outlining the purpose of the study to the potential participants, as well as an informed consent document to be signed by participants. Anonymity and confidentiality was strictly maintained at every stage of the research process without any possibility of being traced back to the participants. No personally-identifying information such as names, e-mail/residential/IP addresses and phone numbers were requested from the participants. Proper data management through coding, storage and security was also employed therefore no link existed between the information collected and the individual participants. Only the principal investigator had access to the data and no potential risks were associated with the study apart from possible discomfort emanating from their lack of awareness to adverse drug reaction reporting protocols, to counteract this, all participants were assured that their responses remain confidential and will never be traced back to them in an effort to undermine their professional status. The collected data was coded, entered into Microsoft® Excel® 2016 and subsequently analysed using SPSS® for IOS version 24.

The data compiled was analysed using descriptive statistics. Correlational techniques were further carried out to analyse the possible relationship between certain variables and ANOVA analysis was also done to investigate if there were significant differences between the different professions in the way that they answered certain questions.

Results

Overview of participant demographics

In total, 103 questionnaires were completed (response rate of 83.7%). The HCPs referred to in this results section are from both hospitals collectively. The respondents comprised 59.4% of females and 40.6% of males. The majority of questionnaires were completed by nurses (n=70, 68%), followed by doctors (n=25, 24.3%) and pharmacists (n=8, 7.8%). The Khomas region hospital accounted for the majority of participants (n=79, 76.7%) in comparison to the Hardap region hospital (n=24, 23.3%). The participants at the Khomas region-based hospital comprised 53 nurses, 6 pharmacists and 20 doctors while the Hardap region-based state hospital constituted of 17 nurses, 2 pharmacists and 5 doctors. Educational qualifications attained for the respondents were as follows: diploma (n=37, 35.9%), postgraduate diploma (n=6, 5.8%), bachelor's degree (n=51, 49.5%), master's degree (n=7, 6.8%) and PhD (n=2, 1.9%).

Most of the HCPs (n=45, 43.7%) had between 1-5 years of experience in practice, followed by those with more than 20 years (n=22, 21.4%), 6-10 years (n=13, 12.6%), 11-20 years (n=12, 11.7%) and lastly HCPs who had less than a year of practice experience (n=11, 10.7%).

Table 1 provides information on the knowledge of HCPs regarding the terminology i.e. "adverse drug reaction", pharmacovigilance" and "spontaneous reporting". Most HCPs could correctly define "adverse drug reaction" (73.8%) while less than half (41.7%) correctly defined "spontaneous reporting".

Table 1: Knowledge of definitions

Adverse drug reaction definition.				
		Incorrect	Correct	Total
Profession	Medical doctor	3 (12%)	22 (88%)	25
	Pharmacist	0 (0%)	8 (100%)	8
	Nurse	24 (34.3%)	46 (65.7%)	70
Total		27 (26.2%)	76 (73.8%)	103
Pharmacovigilance definition.				
		Incorrect	Correct	Total
Profession	Medical doctor	10 (40%)	15 (60%)	25
	Pharmacist	0 (0%)	8 (100%)	8
	Nurse	35 (50%)	35 (50%)	70
Total		45 (43.7%)	58 (56.3%)	103
Spontaneous reporting definition.				
		Incorrect	Correct	Total
Profession	Medical doctor	15 (60%)	10 (40%)	25
	Pharmacist	1 (12.5%)	7 (87.5%)	8
	Nurse	44 (62.9%)	26 (37.1%)	70
Total		60 (58.3%)	43 (41.7%)	103

Sixty point two percent (n=62) of HCPs indicated that they had identified an adverse reaction in practice. Of the 25 doctors who participated, 22 (88%) had identified an adverse reaction in practice whilst 75% of pharmacists (n=6) and 48.6% of nurses (n=34) had identified an adverse reaction before.

Only 36.9% (n=38) of HCPs indicated that they had ever reported an adverse drug reaction. Of the 25 doctors who participated, 8 (32%) had reported an adverse reaction in practice whilst 62.5% of pharmacists (n=5) and 35.7% of nurses (n=25) had reported an adverse reaction. However, nearly all HCPs (n=101, 98.1%) did believe that it was part of their professional obligation to report ADRs.

A total of 48.5 % (n=50) of HCPs correctly identified the safety yellow form as the means to report ADRs in Namibia, but only 36.9% (n=38) knew where to obtain the form from. Only minimal 37.9% (n=39) of HCPs knew the correct regulatory authority in Namibia which is the TIPC that handles ADR report cases, while only 36.9% (n=38) of HCPs pointed out that they had been trained on ADR reporting systems.

In terms of knowledge on causality assessment, less than half of HCPs (n=50, 48.5%) were of the opinion that the pharmacology of the drug can explain the suspected adverse effect and only 68% (n=70) thought it was necessary to know if re-exposure worsens the adverse effect OR withdrawal of the medicine decreases the suspected adverse event.

HCPs were not always clear on which ADRs should be reported – 55.3% (n=57) of HCPs indicated that mild ADRs should be reported and just over half (51.5%, n=53) indicated that ADRs should be reported for herbals and traditional medicines.

HCPs were also unsure of the role of the TIPC; although 65% (n=67) of HCPs were of the opinion that the regulatory authority can withdraw the product from the market only 40.8% (n=42) indicated that a change on the labelling of the product can occur.

Table 2: Summary of awareness and knowledge of healthcare practitioners on adverse drug reaction reporting.

Awareness and knowledge	**Response**	
Identification and reporting of ADRs.	**Number of Respondents**	**Percentage**
I have identified an ADR in practice.	62	60.2
I have reported an ADR before.	38	36.9
It is necessary to report an ADR.	101	98.1
I have received training on ADR reporting systems in Namibia.	38	36.9
Awareness of ADR reporting systems in Namibia.		
Correct knowledge of the safety yellow form for ADR reporting.	50	48.5
Indicated knowledge of where to obtain the safety yellow form.	38	36.9
Indicated awareness of the TIPC as the correct drug regulatory authority.	39	37.9
Knowledge of ADR causality assessment.		
It is important to know all the medication the patient is taking.	93	90.3
It is significantly important to know the timing between administration of the medicine and development of the suspected ADR.	85	82.5
It is important to know if re-exposure or withdrawal of the medicine decreases the suspected ADR.	70	68
It is important to know the pharmacology of the suspect drug.	50	48.5
ADR reporting for which products.		
Herbals and traditional medicines.	53	51.5
Vaccines and medical devices.	94	91.3
Biological and blood products.	82	79.6
Type of ADRs to be reported		
Severe and life-threatening.	101	98.1
Severe and causing disability.	90	87.4
Mild.	57	55.3
Knowledge of what actions the regulatory authority can take.		
Withdraw product from the market.	67	65
Change on product labelling.	42	40.8
Sending out alerts of a possible adverse reaction.	90	87.4
Keep the suspect drug in the market as long as possible.	12	11.7

Further analysis to determine significant relationships and differences

Analysis of results found a statistically significant ($p<0.05$) relationship using correlational analysis between 1) profession and 2) educational qualifications in identifying an adverse reaction in practice. Similarly, training had a positive relation to 1) identifying and 2) reporting adverse drug reactions. Being able to identify and report an ADR was also positively associated to being aware of the safety yellow form.

Multiple comparisons using ANOVA analysis were also done to investigate if there were any significant differences among different professions in their knowledge regarding ADRs and reporting thereof. Significant differences were noted in the way different HCPs responded to certain questions. There was a significant difference ($p<0.05$) between medical doctors and nurses in identifying an adverse reaction in practice. With regards to receiving training on ADR reporting systems, significant differences were noted between medical doctors and pharmacists; medical doctors and nurses; pharmacists and nurses. In relation to knowledge of the safety form, there was a significant difference between pharmacists and medical doctors as well as pharmacists and nurses. Medical doctors and pharmacists along with pharmacists and nurses also significantly differed in knowing where to obtain the safety form. Concerning knowledge of the correct regulatory authority, significant differences were noted between medical doctors and pharmacists as well as pharmacists and nurses.

Discussion

Knowledge of key terms

Doctors, nurses and pharmacists are all collectively responsible for ADR reporting. Comprehension of fundamental terms such as "pharmacovigilance", "adverse drug reaction" and "spontaneous reporting" underpin the ability to discharge this responsibility. The term "adverse drug reaction" was generally well understood yet the knowledge of the terms "pharmacovigilance" and "spontaneous reporting" was generally inadequate. Other research findings [6, 7] also correlate the results of this study were a few HCPs knew the terms "pharmacovigilance" and "spontaneous reporting". The WHO maintains that spontaneous reporting remains the cornerstone of pharmacovigilance [8]. Knowledge of these terms is of the utmost importance otherwise ADR reporting remains subdued. In a previous related study assessing healthcare professionals' pharmacovigilance knowledge, 35.5 % of respondents were not familiar with the term "pharmacovigilance" and limited pharmacovigilance knowledge was cited as the main reason for under-reporting of ADRs [9]. Continuous and rigorous awareness campaigns by the TIPC are vital to sensitize HCPs about how pharmacovigilance plays a major role in the safety monitoring of medicines in clinical practice and how spontaneous reporting remains largely integral to the implementation of this process. Pharmacists displayed resounding knowledge in the definition of all the terms; owing chiefly to the fact that they are better trained in the field of ensuring drug safety.

Under-reporting of ADRs and proposed solutions

The national pharmacovigilance guidelines for medicine safety surveillance, as set out by the MOHSS, underscore spontaneous reporting by HCPs as effective for the Namibian setting in the early detection of unknown problems pertaining to drug safety [3]. Despite 98.1% of HCPs indicating a favourable attitude towards reporting and just over 60% having identified an ADR in practice, only 36.9% had ever reported an ADR before. This is a classic case of serious under-reporting which is widely publicised in various literature [10, 11, 12]. These results are almost similar to a study done at a South African hospital where the vast majority of HCPs indicated ADR reporting is necessary (96.2%) and that it is their professional obligation (89.4%) but the vast majority had never reported an ADR [13].

This study found a significant link between one healthcare profession and the identification of ADRs as more medical doctors identified ADRs in practice as compared to nurses ($p<.001$). This is probably due to medical doctors having a wider knowledge base in the field

of ADR identification as this is taught more in their academic curricula [9]. Nonetheless, there was no significant link in identifying ADRs between pharmacists and medical doctors as both HCPs possess almost the same sphere of knowledge in the discipline of ADR identification as obtained in their undergraduate training [9].

There was no appreciable relationship between the different types of professions and the inclination to report ADRs. As shown by the results of this study, acquiring training on national ADR reporting systems remained the benchmark in having a positive impact on both identifying and reporting ADRs (p=.003). The TIPC and all other relevant stakeholders need to take this into cognizance in their mandate to provide pharmacovigilance training to HCPs. Ideally, the TIPC is supposed to have annual pharmacovigilance trainings however this has been inconsistent in the last five years due to a lack of funds. One training session was conducted in 2017 and another one was co-ordinated in 2019 as well. Health personnel do not stay the same, there is always a natural progression of HCPs moving and being replaced by those who have not necessarily been trained on ADR reporting before. Interactive methodical educational sessions on pharmacovigilance can be utilized in an effort to engage HCPs and online training material (including audio-visual material, electronic publications and email reminders) can be made available for ease of reference. Several studies [14, 15] have documented how HCPs better understood ADR reporting after the implementation of several educational interventions. HCPs in southern India were involved in the pre-KAP (Knowledge, Attitude, Practice) questionnaire, an educational intervention, and a post-KAP questionnaire. Following the educational intervention, ADR reporting doubled compared to pre-intervention [16].

The Health Professions Council of Namibia (HPCNA) requires every registered HCP to obtain a certain number of continuing education units (CEUs) every 12 month period as part of continuing professional development (CPD). At least 5 of these CEUs should be for ethics, human rights and medical law [17]. In light of the finite knowledge on ADR reporting as a whole, it might be prudent to allocate a few requisite CEUs on pharmacovigilance in order to better equip HCPs on this issue. This would create a chain in which lives and resources are saved from the dis-benefit arising from HCPs who are oblivious to the identification and reporting of ADRs.

The Pharmacy Council of Namibia is involved in the development and ongoing review of the academic curriculum for pharmacy students at local universities. The equivalent also applies

to the Medical and Dental Council for doctors and the Nursing Council for nurses. In addition to HCPs being taught about pharmacovigilance at institution level, equal emphasis should also be placed on familiarisation with national guidelines on ADR reporting and not just on internationally accepted standards. It is worth pointing out that nurses are likely to see more patients and identify more ADRs when doctors are unreachable hence their training on ADR reporting should not be trivialized [9].

Under-utilization of safety yellow form reporting

The safety yellow form is wholly used as the reporting tool available at state health facilities in the country. The forms are mostly kept at the pharmacy dispensaries as the focal point and at some wards and consulting rooms. Less than half of HCPs (48.5%) correctly identified the form used to report ADRs in Namibia, furthermore, only 36.9% knew where to obtain the form from. These findings are of huge concern. A 2018 study conducted in Turkey also revealed that only 34.7% of HCPs knew where to find the ADR reporting form, and 25.5% had previously filled the form and/or read it [18].

The results obtained in this study correlated knowledge of where to obtain the safety yellow form with identification ($p=.010$) and reporting ($p<.001$) of ADRs. The TIPC, in conjunction with hospital management, should make sure that HCPs are aware of the safety yellow form. Moreover, supplemental efforts are needed to increase knowledge of where the forms are obtained otherwise reporting of ADRs will remain extremely diminished. Department heads should ensure continual availability and visibility of forms in their respective wards rather than from only one central collection point. Pharmacists, as custodians of medicines, showed unparalleled knowledge of the safety form; this is chiefly because the TIPC keeps the majority of the forms at the dispensaries. On that account, pharmacists can be used as the focal point to inform their professional colleagues about the availability of the safety yellow forms in an effort to encourage more ADR reporting.

Healthcare professionals' general awareness and knowledge on ADR reporting

As the drug regulatory unit of the country, the TIPC is relentlessly involved in improving the rational and safe use of medicines in Namibia. All ADR reports and pharmacovigilance services to both the public and HCPs are solely handled by the TIPC. At best, only 37.9% of HCPs knew about the TIPC and were further unfamiliar with the actions that the TIPC can take upon receiving reports of suspected ADRs. In line with these actions, a pharmaceutical product can be withdrawn from the market; only 65% of HCPs knew this. A change in the labelling of

the product to inform healthcare practitioners and consumers of the possible adverse effect is also plausible but a reluctant 40.8% of HCPs were aware of this. This is fundamental knowledge that all HCPs need to have so that they can swiftly react to circulars from the TIPC pertaining to urgent actions that may need to be undertaken. A study on post-marketing withdrawal of medicinal products concluded that withdrawal of products following reports of suspected adverse reactions, sufficiently serious to affirm withdrawal, has not improved consistently over the last few decades and that harmful drugs are less likely to be withdrawn in African countries due to lack of knowledge and urgency by HCPs to respond to mandates from the regulatory authorities [19]. Moreover, a reduction of ADRs rests on the awareness of HCPs to taking heed of subsequent safety-related label revisions [20].

Causality assessment of ADRs is a method used for estimating the strength of a relationship between drug(s) exposure and the occurrence of ADRs in order to aid signal detection and risk–benefit decisions regarding medicines [21]. Overall, HCPs had adequate knowledge of causality assessment. The only perceptible concern in the study was that 48.5% of HCPs are not of the opinion that the pharmacology of a drug can explain the suspected adverse effect but it is well known that certain ADRs can be predicted by a drug's mechanism of action [21]. This is significant in helping HCPs to better predict and identify ADRs in real practice.

ADR severity describes the extent to which the ADRs influence the everyday life of the patients [21]. All HCPs unanimously agreed that severe life-threatening ADRs and those causing disability should be reported. However, 55.3% do not believe that mild ADRs should be reported. A study in Ethiopia also established that a significant proportion of HCPs replied that ADRs should be reported only when they are serious and life-threatening and severe and cause disability [7]. As much as mild ADRs do not severely affect a patient's life and might not require the complete withdrawal of the drug concerned, they need to be reported too.

The seriousness of an ADR is related to its life-threatening nature and this can result in far-reaching consequences such as hospitalization, congenital abnormality and even death of a patient. The NMRC guidelines set out that ADR reporting should be done for every pharmaceutical product including vaccines, medical devices, blood/biological products and herbals/traditional medicines. Just about half of all HCPs (51.5%) indicated that ADRs should be reported for herbals and traditional medicines. More knowledge needs to be disseminated on the need of taking herbals and traditional medicines into consideration when taking the history of a patient whenever an ADR is suspected. In our cultural settings, many people tend

to self-medicate at home with well know traditional medicines and herbs and this can have a profound impact on other concomitantly administered drugs. Traditional medicines can be effective but that is not to say they are completely harmless [22].The safety of many medicinal plants used in traditional medicines has been the focus of many studies [22, 23].

Conclusion

This study was conducted in an effort to ascertain if HCPs have awareness and knowledge of ADR reporting systems in Namibia. While the results found HCPs knowledgeable on certain aspects, it also alluded to the under-reporting of ADRs. The TIPC needs to explore measures in order to educate HCPs on pharmacovigilance so that they are better equipped not just to identify ADRs, but to report them as well. Awareness of the availability and location of safety yellow forms remains equally predominant as this is the reporting tool. Various stakeholders in the health sector and government agencies need to come on board in order to unitedly fortify pharmacovigilance systems among HCPs in Namibia.

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CHAPTER 4
CONCLUSIONS

4.1 **Introduction**

This study was carried out to assess awareness and knowledge of HCPs in Namibia regarding ADR reporting procedures. The rationale of this study was based on previous research conducted in Namibia which highlighted that half of the HCPs in the country were not aware of any ADR reporting systems in place, nor had knowledge on how to report ADRs to the TIPC [1]. In the case of this study, less than half of all HCPs in the country did not have awareness and knowledge of ADR reporting systems in the country. This lack of awareness is not unique to Namibia alone, it is also well documented in other countries [2]. In line with one of the many recommendations from these precursory studies, this research was done in the public sector to ascertain the immensity of this awareness and knowledge among HCPs.

4.1.1 **Strengths of the study methodology and design**

The self-administered questionnaires used in the study were easy to follow without any supervision from the principal investigator. Furthermore, this study yielded findings with minimal costs incurred due to the simplicity of the research tool which was effortlessly distributed among the HCPs. In an effort to maintain validity, the questionnaire was first piloted to 10 HCPs to remove any possibility of questionnaire irrelevance and of seemingly straightforward questions being open to a number of interpretations. The consensus from the pilot group was in line with the simplicity and clarity of the research tool.

Since this study was quantitative and restricted to specific HCPs at the two state hospitals, the response rate was good (83.7%). Data was relatively easy to further analyze so as to deduce certain trends and differences among the HCPs in relation to different variables.

4.1.2 **Limitations of the study**

- The outcome of this study may not be generalized to other HCPs in the country.
- More public hospitals will have to be surveyed to enable proper and more diverse recommendations for increased ADR reporting awareness and knowledge.
- Expert sampling could have introduced bias were HCPs felt they needed to respond to questions in a certain way in line with the researcher’s expectations.

4.2 **Conclusions drawn from the study findings**

The aim of this study was to assess awareness and knowledge of doctors, pharmacists and nurses in Namibia regarding ADR reporting systems. To achieve this, HCPs were questioned to determine the following:

1. If they understood the term adverse drug reaction and if they had ever encountered it before in practice. Knowledge of the terms pharmacovigilance and spontaneous reporting was also investigated as well.
2. If they thought it was necessary to report an ADR and if they deemed it as their professional obligation to do so.
3. Awareness of the TIPC which handles ADR reporting.
4. Any knowledge of the safety yellow forms for ADR reporting which are available at the facilities.
5. Any training on national ADR reporting systems.
6. Knowledge of how to identify ADRs in practice and the processes which occur after submission of the safety yellow form.

Conclusions drawn from the study findings based on the above research questions

- Most HCPs (73.8%) could correctly define "adverse drug reaction"; an average number (60.2%) had identified an ADR in practice while less than half (41.7%) were subpar in correctly defining "spontaneous reporting". Only 56.3% correctly defined "pharmacovigilance". Comprehension of fundamental terms such as "spontaneous reporting" and "pharmacovigilance" among HCPs was not enough and this could adversely affect the ability to report ADRs or recognize the importance of reporting ADRs. Pharmacists demonstrated a higher level of knowledge of these key terms as the custodians of medicine.
- A majority (98.1%) of HCPs deemed it necessary as part of their professional obligation to report ADRs, but only 36.9% had actually reported an ADR before resulting in profound under-reporting. Undetected ADRs due to under-reporting can have far-reaching consequences with regards to compromised drug safety.
- Awareness and knowledge of ADR reporting systems in Namibia among HCPs was low. Thirty seven point nine percent of HCPs indicated awareness of the TIPC as the correct drug regulatory authority and were oblivious to some of the important actions the TIPC could institute following the submission of an ADR report. Forty-eight and a half percent had correct knowledge of the safety yellow form for ADR reporting and 63.1% did not know where to obtain this form. This lack of knowledge was potentially due to the fact that only

36.9% had received training on ADR reporting systems which is highly inadequate. Further analysis revealed that training and knowledge of where to obtain the safety yellow form is beneficial in identifying and reporting ADRs.

- The majority of HCPs (84%) were fairly knowledgeable with regards to causality assessment to identify ADRs. Satisfactory awareness of ADR severity and seriousness was noteworthy although supplemental training will always be needed to complement the knowledge that already exists.

4.3 **Significance of the study**

- The results of this study give an indication to the extent to which HCPs in Namibia are aware of ADR reporting systems in the country with the aim to detect and minimize the occurrence of ADRs. ADRs are a major cause of patient-related morbidity and mortality and awareness of HCPs to ADR reporting systems in Namibia will play a huge role in effective and safe clinical practice [3].
- The TIPC as the drug regulatory authority of the country could use the outcome of this study to design robust intervention methods and awareness campaigns required to increase or improve ADR reporting awareness among HCPs. Accordingly, the TIPC will also be able to utilize the outcome of this study to strengthen pharmacovigilance systems as a mandate to the Namibian government in ensuring the national provision of medicines which are safe, effective and of good quality.

4.4 **Recommendations**

- Awareness and training programs designed to improve reporting behavior among HCPs need to be implemented by the TIPC in an effort to address the under-reporting of ADRs. However, the TIPC alone cannot undertake this engagement. Various stakeholders in the health fraternity, including multiple government agencies, need to come on board in a show of support to make sure that the TIPC fulfills its ordinance.
- Pharmacovigilance tutelage needs to be incorporated into the academic curriculum for all medical doctors, nurses and pharmacists as the responsibility for ADR reporting is not just confined to a single profession. The HPCNA can also aid in the incorporation of mandatory pharmacovigilance CEUs as part of the CPD program for all HCPs.
- The safety yellow form is the reporting tool available in the public health facilities. HCPs need to be well informed about how to use this form and where to find it; this can also be

done during the orientation of new staff members as well. The availability of the safety yellow forms for all hospital departments in clearly marked locations is a requisite.

- Pharmacists should be utilized as the focal point in pharmacovigilance implementation as they displayed better dexterity in the knowledge of ADR reporting systems. The TIPC can make use of at least one pharmacist already based in that particular facility as a pharmacovigilance officer.
- The TIPC needs to routinely update its website and encourage the use of the online ADR form submission function in order to enhance electronic reporting.

4.5 **Chapter summary**

This final chapter highlighted the conclusions drawn from the findings of the study, described the significance, strengths and limitations of the study, as well as provided recommendations for improving awareness and knowledge among HCPs to ADR reporting systems in the country.

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ANNEXURE 1

Ethical approval obtained from the University of KwaZulu-Natal

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

30 September 2019

Mr G Ndlovu (217081299)
School of Health Sciences
College of Health Sciences
garnetndlovu@yahoo.co.uk

Dear Mr Ndlovu

Protocol: Awareness and knowledge of doctors, pharmacists and nurses on adverse drug reaction reporting systems in Namibia - A study at two state hospitals in the Khomas and Hardap regions
Degree: MHSc
BREC Ref No: BE489/19

EXPEDITED APPLICATION: APPROVAL LETTER

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 30 July 2019.

The study was provisionally approved pending appropriate responses to queries raised. Your response received on 16 September 2019 to BREC letter dated 06 September 2019 has been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have been met and the study is given **full ethics approval** and may begin as from 30 September 2019. **Please ensure that outstanding site permissions are obtained and forwarded to BREC for approval before commencing research at a site.**

This approval is valid for one year from **30 September 2019.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **noted** by a full Committee at its next meeting taking place on **12 November 2019.**

Yours sincerely

Prof V Rambiritch
Chair: Biomedical Research Ethics Committee

CC: Postgrad admin: nenep1@ukzn.ac.za Supervisor: oosthuizenf@ukzn.ac.za

Biomedical Research Ethics Committee
Professor V Rambiritch (Chair)
Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Telephone: +27 (0) 31 260 2486 **Facsimile:** +27 (0) 31 260 4609 **Email:** brec@ukzn.ac.za
Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

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ANNEXURE 2

Ethical approval letter obtained from the Ministry of Health and Social Services in Namibia

REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

Private Bag 13198
Windhoek
Namibia

Ministerial Building
Harvey Street
Windhoek

Tel: 061 – 203 2537
Fax: 061 – 222558
E-mail: btjivambi@mhss.gov.na

OFFICE OF THE EXECUTIVE DIRECTOR

Ref: 17/3/3 GD
Enquiries: Mr. B. Tjivambi

Date: 21 May 2019

Mr. Garnet Ndlovu
PO Box 1168
Mariental
Namibia

Dear Mr. Ndlovu

Re: Awareness and Knowledge of Doctors, Pharmacist and Nurses on adverse drug reaction reporting systems in Namibia-study at two State Hospitals in the Khomas and Hardap Regions

1. Reference is made to your application to conduct the above-mentioned study.

2. The proposal has been evaluated and found to have merit.

3. **Kindly be informed that permission to conduct the study has been granted under the following conditions:**

3.1 The data to be collected must only be used for academic purpose;

3.2 No other data should be collected other than the data stated in the proposal;

3.3 Stipulated ethical considerations in the protocol related to the protection of Human Subjects should be observed and adhered to, any violation thereof will lead to termination of the study at any stage;

3.4 A quarterly report to be submitted to the Ministry's Research Unit;

3.5 Preliminary findings to be submitted upon completion of the study;

3.6 Final report to be submitted upon completion of the study;

3.7 Separate permission should be sought from the Ministry for the publication of the findings.

4. All the cost implications that will result from this study will be the responsibility of the applicant and **not** of the MoHSS.

Yours sincerely,

PERMANENT SECRETARY
MINISTRY OF HEALTH & SOCIAL SERVICES

MR. BEN NANGOMBE
EXECUTIVE DIRECTOR

"Health for All"

ANNEXURE 3

Safety yellow form used in Namibia

Ministry of Health and Social Services

ADVERSE MEDICINE REACTION REPORTING FORM

A) PATIENT INFORMATION

Patient initials or Hospital Reg. No.		DOB Age.....	Gender: ☐ Male ☐ Female	Weight (Kg):	*Safety Yellow Form* *Confidential*

B) ADVERSE EVENT INFORMATION

Type of report: **Initial:** ☐ **Follow up:** ☐ Write AMR ID number

DESCRIPTION OF ADVERSE EVENTS: Indicate provisional/final diagnosis of the adverse event	**Date the event started:**	**Date the event stopped:**	**Action taken:** (E.g. Medicine withdrawn/ substituted/Dose reduced /medical treatment etc...)

Seriousness	☐ Hospitalization ☐ Life-threatening	☐ Disability or permanent damage ☐ Other serious medical event	☐ Congenital anomaly/ birth defect ☐ Non serious adverse event

Relevant Laboratory tests	**Test date**	**Result**

Patient Outcome	☐ Recovered ☐ Recovered with sequela ☐Recovering ☐ Not recovered ☐ Unknown	**Died** ☐Due to reaction ☐ Reaction maybe contributory ☐ unrelated to reaction Date of death

RELEVANT MEDICAL HISTORY: including pre-existing medical conditions (allergies, pregnancy, alcohol use, liver problems..)

C) INFORMATION ON MEDICINES: *For vaccines please indicate the batch number*

LIST MEDICINES USED IN THE LAST 3 MONTHS TICK SUSPECTED MEDICINES ENTER FDC AS ONE MEDICINE		Strength	Frequency	Route of Admin.	Start date	Stop date or ongoing	Indication
	☐						
	☐						
	☐						
	☐						
	☐						
	☐						

D) REPORTER INFORMATION

Name (last, first)		Region		Email	
Profession		Telephone		Date	
Health Facility Name		Fax			

Please tick if you need ☐ *AMR forms* ☐ *Additional information*

Please note that submission of a report does not constitute an admission that medical personnel or the medicine caused or contributed to the event

Send/ Fax/Email to TIPC: Therapeutics Information and Pharmacovigilance Centre
Room 21, Basement Area, Windhoek Central Hospital. Windhoek.
Tel: 061 203 2312 Fax: 061 22 66 31/ 088 618 776. Email: info@tipc.com.na

ANNEXURE 4

Research Questionnaire

Questionnaire

1) Profession

□ Medical Doctor □ Pharmacist □Nurse

2) Gender

□ Male □ Female

3) Educational qualifications attained?

□ Diploma

□ Postgraduate Diploma

□ Degree

□ Masters Degree

□ PhD

4) Number of years in practice?

□ Less than a year

□ 1-5 years

□ 6-10 years

□ 11-20 years

□ More than 20 years

5) What do you understand under by the term “Adverse Drug Reaction?”

_____
_____
_____
_____
_____
_____

6) What do you understand by the term “Pharmacovigilance?”

_____
_____
_____
_____
_____
_____

7) What do you understand from “Spontaneous reporting” of adverse effects of medicine?

_____
_____
_____
_____
_____
_____

8) Which of the following do you need to know when you need to decide if an effect was caused by a medicine? (Choose all appropriate options)

□ Know all the medication the patient is currently taking.

□ Know the timing between administration of the medicine and development of the suspected adverse effect.

□ Know if re-exposure worsens the suspected adverse effect OR withdrawal of medicine decreases the suspected adverse effect?

□ Know that the pharmacology explains the suspected adverse effect?

9) ADRs should be reported for which of the following products? (Choose all appropriate options)

□ Herbals and traditional medicines.

□ Vaccines and medical devices.

□ Biological and blood products.

□ Only prescribed medicines with a low therapeutic index.

10) Which types of ADRs should be reported? (Choose all appropriate options)

□ Severe and life threatening.

□ Severe and causing disability.

□ Mild and cause less.

11) Do you believe clinical trials during medicine development are sufficient to identify ALL adverse effects a medicine might have?

□ YES □ NO

12) Which of the following might be the result of an adverse effect caused by a medicine? (Choose all appropriate options)

□ Hospitalization.

□ Life threatening situation.

□ Congenital abnormality.

□ Death of a patient.

13) Have you ever identified an adverse reaction in practice?

□ YES □ NO

14) Have you ever reported an adverse drug reaction?

□ YES □ NO

If you answered YES, WHO did you report the adverse drug reaction to?

…….

15) Do you believe it is necessary to report an ADR?

□ YES □ NO

16) Have you ever been trained on how to report an ADR?

□YES □ NO

17) Have you ever, formally or informally, been informed about systems for ADR reporting in Namibia?

□ YES □ NO

18) What is the report form used to report adverse drug reactions in Namibia?

□ Medwatch form.

□ Sentinel event reporting form.

□ Safety yellow form.

19) Do you know where to obtain the form in (18)?

□ YES □ NO

20) Who must you submit this form to?

□ Monitoring centre for therapeutics Namibia.

□ Namibia pharmacovigilance monitoring centre.

□ Therapeutics information and pharmacovigilance centre.

21) Which of the following can the regulatory authority do based on reports of adverse drug reactions reported to them? (Choose all appropriate options)

□ Withdraw the product from the market.

□ Change on the labelling of the product to inform healthcare practitioners / consumers of the possible adverse effect.

□ Send out alerts to prescribers and consumers to inform them of a possible adverse reaction.

□ Keep the suspect drug in the market despite the adverse effects for as long as possible provided its patent is still active.

22). Who is responsible for ADR Reporting? (Choose all appropriate options)

□ Doctors □ Pharmacists □ Nurses

ANNEXURE 5

Information sheet and consent to participate in research study

Date: 01/10/2019

Dear Healthcare Professional

My name is Garnet Ndlovu and I am a postgraduate student in the College of Health Sciences at the University of Kwazulu-Natal in South Africa.

You are being invited to participate in a study investigating knowledge of healthcare professionals about adverse drug reaction reporting systems in Namibia. The study will expect you to complete a questionnaire with questions related to adverse reactions and the reporting of these in Namibia. We hope that the study will provide insight into how to improve and strengthen pharmacovigilance systems which are needed to ensure drug safety.

This study does not involve any risks.

This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval number BE 489/19).

In the event of any problems or concerns/questions you may contact me on 0817550358 or by email garnetndlovu@yahoo.co.uk or the UKZN Biomedical Research Ethics Committee, contact details as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Participation in this research is voluntary and participants may withdraw participation at any point, and that in the event of refusal/withdrawal of participation the participants will not incur penalty.

All the information collected will remain confidential without any possibility of being traced back to the participant.

CONSENT

I……..have been informed about the study entitled 'Awareness and knowledge of doctors, pharmacists and nurses on ADR reporting systems in Namibia - a study at two state hospitals in the Khomas and Hardap regions' by the researcher Garnet Ndlovu.

I understand the purpose and procedures of the study.

I have been given an opportunity to answer questions about the study and have had answers to my satisfaction.

I declare that my participation in this study is entirely voluntary and that I may withdraw at any time without affecting any care that I would usually be entitled to.

If I have any further questions/concerns or queries related to the study I understand that I may contact the researcher on 0817550358 or by email at garnetndlovu@yahoo.co.uk

If I have any questions or concerns about my rights as a study participant, or if I am concerned about an aspect of the study or the researchers then I may contact:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

_____ _____
Signature of Participant **Date**

_____ _____
Signature of Witness **Date**
(Where applicable)

_____ _____
Signature of Translator **Date**
(Where applicable)

ANNEXURE 6

Author guidelines for manuscript publication: Journal of pharmacy practice

Pharmacy Practice supports and is supported by the fundamentals of scholarly publishing. Authors considering submit a paper to **Pharmacy Practice** must follow a strict code of conduct based on the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals, especially on regards Roles & Responsibilities and the Scientific Misconduct of the authors and collaborators.

- Originality of the text in manuscripts is checked by the text-similarity detection service Crossref Similarity Check.
- Correspondence author is responsible of including all the authors that granted the right to be author, but also to not include any individual who does not deserve the authorship. Notwithstanding, Pharmacy Practice has no limit in the number of authors per paper, we recommend double checking the criteria to consider a contributor as an author, and also to consider if the role of Collaborator or a simple acknowledgement are more appropriate.
- If a scientific misconduct is suspected, COPE flowcharts will be applied with no restriction, as we did in the past (Pharm Pract (Granada) 2012;10(1):1-2).

Authors are encouraged to visit the Instructions for Reviewers to see how these crucial collaborators should evaluate the manuscript.

Additional recommendations, applicable to any category of articles:

- Abstract should have no more than 350 words and no less than 250 (in Original research articles, abstracts should be structured in Background, Objective, Methods, Results, and Conclusion).
- Only Keywords based on NLM Medical Subject Headings are used.
- References should be cited in the main text as numbers in superscript at the end of sentences (always after the period). The list of references should be numbered and ordered as they were cited in the text.
- Reference format should follow ICMJE recommendations (Citing Medicine) and journal titles must be abbreviated according to the MEDLINE style, available at the NLM Catalog.
- Tables must appear at the end of the text, formatted as follows:
    -
        - Use simple grid without merging cells. No cells shading is allowed.
        - Font must be Calibri 8pt; line spacing: simple.
        - Orientation of the page containing the table must be: portrait.
        - Table should fit into one page. Oversized tables will be moved to online appendix.
- Figures are preferred pasted as Microsoft Objects. Color use should take into account that papers can be printed in black and white.
- Avoid the abuse of abbreviations. Use only abbreviations commonly accepted. Do not create new abbreviations.

- Avoid the use of non-common Roman characters. Do not use Greek letters into the text (they can be used in equations). Do not use special characters like ± ½ ¼ or arrows.
- Present standard deviations as (SD=2.34), and confidence intervals as [95%CI 2.36:4.23]
- For currency abbreviations, use the ISO 4217 codes.
- Follow International standards for author's names and abbreviations. John Philip Doe will be abbreviated as Doe JP. Download here an Excel file to see how your name will be abbreviated following International standards.
- **[NEW RULE for 2020]** Provide only one institution for each author's affiliation. Affiliations must be translated into English (no exceptions to this rule). Candidate positions are not considered.
- For non-native English authors, a scientific editing service could be required. See below a list of some of these scientific editing providers. Authors using this service should include a sentence in the acknowledge section.

ANNEXURE 7

Journal submission letter