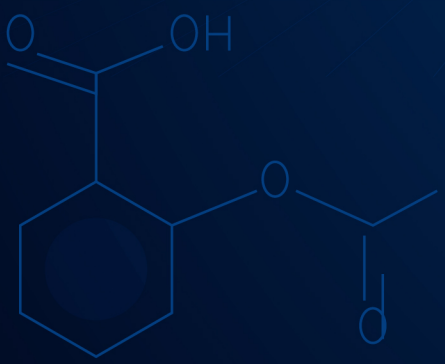
AMERICAN JOURNAL OF
CHEMISTRY AND PHARMACY (AJCP)
ISSN: 2834-0116 (ONLINE)
VOLUME 3 ISSUE 1 (2024)



PUBLISHED BY
E-PALLI PUBLISHERS, DELAWARE, USA

American Journal of Chemistry and Pharmacy (AJCP)

Volume 3 Issue 1, Year 2024
ISSN: 2834-0116 (Online)
DOI: https://doi.org/10.54536/ajcp.v3i1.3197
https://journals.e-palli.com/home/index.php/ajcp

Adverse Drug Reactions in Nigeria's Geriatric Population and its Prevalence, Etiologies, Implications: A Systematic Review

Uyiose Fortress Ufuah[1], Aloysius Obinna Ikwuka[2*], Angus Nnamdi Oli[3], Brian Ogbonna[3]

Article Information

Received: July 23, 2024
Accepted: August 18, 2024
Published: August 21, 2024

Keywords

Adverse Drug Reactions, ADRs, Nigeria, Geriatric, Population, Prevalence, Etiologies, Implications, Systematic Review

ABSTRACT

Adverse drug reactions (ADRs) are a significant public health concern. Although the prevalence of ADRs in the general adult population in Nigeria has been studied and documented, there is limited research on ADRs among the geriatric population. This study conducted a systematic review of existing research to determine the prevalence, etiologies and implications of ADRs among Nigerian geriatric population. A comprehensive search was undertaken using PubMed, ResearchGate, and Google Scholar databases. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline was used for reporting this systematic review. Six studies met the eligibility criteria for inclusion in this review. The prevalence of ADRs among the geriatrics ranged from 4.4% to 31.1%. The gastrointestinal system was the most commonly affected system, with non-steroidal anti-inflammatory drugs (NSAIDs) being the most frequently implicated class of drugs contributing to ADRs. The prevalence of ADRs in the Nigerian geriatric population is underreported. There are insufficient policies and healthcare personnel specialized in caring for geriatric patients. Strategies should be implemented to reduce the incidence of ADRs among geriatric patients.

INTRODUCTION

The health and well-being of the elderly have become significant concerns in public health. Globally, the population is aging rapidly, resulting in a decline in health as individuals grow older. In developing countries, the elderly population faces significant morbidity and disability burdens due to poverty, inadequate health facilities, and insufficient care policies. The geriatric population defined as individuals aged 65 and above, is considered a special population as they differ greatly from other age groups. They are more vulnerable to co-morbidities, drug interactions, polypharmacy, and adverse drug reactions (ADRs) (WHO, 2019).

Diabetes mellitus and arterial hypertension remain two of the most common diseases in the world. Today, diabetes mellitus (DM) ranks third in the overall structure of morbidity and mortality after cardiovascular diseases and oncological diseases (Virstyuk & Ikwuka, 2021a). Moreover, the nexus, pathogenetic mechanisms, roles, and effects of metabolic syndrome diseases on aging (and vice versa) are still being investigated by different researchers.

Metabolic disorders, e.g. Hypertension, Adiposity, Diabetes mellitus and Dyslipidemia, collectively known as Metabolic Syndrome Diseases (MSDs) are diseases related to one another (Ikwuka, 2015; Ikwuka, 2017a; Ikwuka, 2017c; Ikwuka & Virstyuk, 2023c; Ikwuka *et al.*, 2023f; Virstyuk *et al.*, 2016). T-helper 17 (Th17) cells secrete interleukin-17 (IL-17) which act on fibroblasts and endothelial cells to increase inflammation (Ikwuka, 2023b). Different studies have shown that MSDs are associated with asymptomatic hyperuricemia, systemic immune inflammatory processes, and fibrogenesis all of which can lead to nephropathy (Ikwuka & Haman, 2017d; Ikwuka *et al.*, 2017e; Ikwuka, 2018c; Ikwuka & Paliy, 2018d; Ikwuka, 2019a; Ikwuka & Virstyuk, 2019c; Ikwuka & Virstyuk, 2022; Ikwuka *et al.*, 2023d; Virstyuk & Ikwuka, 2017a; Virstyuk & Ikwuka, 2018a; Virstyuk & Ikwuka, 2019; Virstyuk & Ikwuka, 2021a; Virstyuk e*t al.*, 2021b) and different rheumatological disorders in the elderly e.g. gouty arthritis, osteoarthritis, etc.

Thus, age is an independent risk factor for chronic non-communicable diseases, which have high morbidity and mortality rates (Jaspinder *et al.*, 2014). Aging is associated with increasing oxidative stress. Linked to the induction of oxidative stress are major free radicals. Among these major free radicals, superoxide anions, hydroxyl radicals, and hydroperoxyl radicals are of physiological significance. A non-radical of physiological significance is hydrogen peroxide (Ama *et al.*, 2023; Baysah *et al.*, 2023; Ekechi *et al.*, 2023a; Uche *et al.*, 2023).

Increased oxidative stress can lead to mutation which is an alteration in the DNA sequence which produces new alleles. One common type of single gene mutation is the missense mutation which results in the substitution or replication of a single amino acid in the polypeptide chain e.g. sickle cell disease is caused by a missense mutation that produces a substitution of valine for glutamate in the two β-globin polypeptide chains (Ikwuka, 2023a; Musa *et al.*, 2023). Sickle cell disease is characterized with different severities of anemia (Inya *et al.*, 2023a; Inya *et al.*, 2023b). Research also shows that disorders in individuals aged 60 and above, account for 23% of the global disease burden (Prince *et al.*, 2015). 60 years and above is also a risk factor for the development of different myelo- and lymphoproliferative disorders such as myelodysplastic

[1] Faculty of Pharmacy, University of Ibadan, Ibadan, Nigeria
[2] College of Medicine and Health Sciences, American International University West Africa, Banjul, The Gambia
[3] Faculty of Pharmacy, Nnamdi Azikiwe University, Awka, Nigeria
[*] Corresponding author's e-mail: momohshaibu3@gmail.com

syndrome, multiple myeloma, and non-Hodgkin lymphoma (Ikwuka, 2023e). Therefore, there is a high demand for health services to meet the needs of this age group, requiring special attention to their treatment process (Davies & O'mahony, 2015).

In addition, there is also a need for new and effective treatment options in patients with Metabolic Syndrome Diseases. Sodium-Glucose Linked Transporter 2 (SGLT-2) inhibitors e.g. Dapagliflozin and Glucagon-like Peptide 1 Receptor Agonists (GLP-1 RAs) e.g. Liraglutide have been found to improve the efficacy of treatment and clinical course of type 2 diabetes mellitus and hypertension in patients with such comorbidities (Ikwuka, 2017b; Ikwuka, 2018a; Ikwuka, 2018b; Ikwuka, 2019b; Ikwuka & Virstyuk, 2021; Ikwuka, 2024; Virstyuk *et al*., 2017b; Virstyuk *et al*., 2018b; Virstyuk & Ikwuka, 2018c). It has also been reported that coconut water has hepatorenal protective functions against alloxan-induced type 1 diabetes mellitus (Ekechi *et al*., 2023b).

Adverse drug reaction (ADR) is defined as "an appreciably harmful or unpleasant reaction resulting from the use of a medicinal product; adverse effects usually predict future hazards and require prevention, specific treatment, alteration of dosage regimen, or withdrawal of the product" (Aronson & Ferner, 2005). ADRs are common in clinical practice, with some cases being severe and leading to unscheduled hospital admissions and even death (Coleman & Pontefract, 2016; Alhawassi *et al*., 2014).

Adverse drug reactions in the geriatric population pose a significant problem in managing elderly patients. This is due to the decline in physiological functions (such as decreased renal and hepatic clearance), co-morbidity, pharmacodynamic and pharmacokinetic changes, frailty, polypharmacy, and memory problems commonly observed in this population. Multiple drug therapies for co-morbidities increase the risk of drug interactions and inappropriate medication prescribing. Studies have shown that prescription medication use among elderly patients has doubled in recent years (Charlesworth *et al*., 2015).

The prevalence of ADRs in older adults has been documented in African countries with several studies highlighting the major drug classes responsible for ADRs. However, global studies on the prevalence of ADRs in the general adult population are more extensive than those focused on the elderly population, despite their higher susceptibility to ADRs (Alhawassi *et al*., 2014; Saka *et al*., 2017; Mekonnen *et al*., 2018; Zazzara *et al*., 2021).

Systematic reviews conducted on the prevalence of adverse drug reactions in elderly patients in other parts of the globe reported ADR prevalence of 11%-22% (Alhawassi *et al*., 2014; Jennings *et al*., 2020; Yadesa *et al*., 2021). There is paucity of systematic reviews conducted on the elderly in Africa. A systematic review on ADRs in both children and adults in African hospitals reported that 8.4% of patients have experienced an adverse drug reaction at hospital admission while 2.8% of admissions were caused by adverse drug reactions (Mekonnen *et al*., 2018). In Nigeria, very few studies focused on the general adult population with none on the geriatric population that suffers ADRs the most. Therefore, this study aimed to systematically review the published literature to determine the prevalence, etiologies, and implications of ADRs in the Nigerian geriatric population.

METHODOLOGY

Information Sources

Online databases and PROSPERO were searched initially to ensure that the review topic had not been researched earlier. When that was established, the research question, selection strategy, and selection criteria were defined. The data collection form was designed in Microsoft Excel, the search strategies were run in the databases, and all references and abstracts were collected in a single file. Search strings were constructed using Boolean Operators ANDs and ORs. Using subject headings obtained from journals and databases, reference lists for primary literature, grey literature and proceedings from conferences were obtained.

Question Structure

The population (geriatric/elderly) and clinical outcomes (ADRs, drug therapy problems) were considered. Prevalence studies and those focusing on the challenges of ADRs were also considered.

Search Strategy and Selection Process

Results from the searches revealed 100 studies. A total of 87 articles on ADR in specific diseases, in other African countries, on polypharmacy, and potentially inappropriate medications (PIMs) were eliminated leaving 13 studies on ADR in the elderly in Nigeria. 4 duplicate studies and 3 incomplete texts were eliminated which gave rise to 6 studies that met the inclusion criteria (see Figure 1).

Inclusion Criteria and Its Reliability

Articles were selected for the review if they: (1) are research articles reporting primary data collected by the authors; (2) are published in English and full-text articles were available; (3) cover geriatrics in Nigeria; and (4) studied populations are 60 years or older. Cohen Kappa statistics was used to discuss and resolve disagreements between the authors who reviewed the articles during selection (Cohen, 1968).

Exclusion Criteria

All studies on geriatric ADRs in Nigeria with incomplete information on study methods or unclear methodology were excluded, including studies without comprehensive summaries.

Data Extraction

Eligible studies and literature were assessed using two parallel reviewers who utilized the eligibility criteria consistently. All data on authors and year conducted, age range, setting/geographical zone, study design,

prevalence, medications implicated, system, and organ most implicated in ADRs of the population were extracted to form the evidence-based table. Data was summarized using Microsoft Excel. Comparisons of extracted data were made and disagreements were resolved with sensitivity analysis, predominantly by further investigation and arbitration.

Data Items (Outcomes)

Data items on ADRs among geriatrics covering 1980 to 2022 were searched. The geriatric population was searched. However, elderly and older adults were also searched in parallel and in series. The etiologies of ADRs and their implications were also searched.

Publication Risk of Bias Assessment

Grey literature and conference proceedings scanning were utilized, in addition to the careful use of search terms in parallel and in series to minimize the risk of bias.

Quality Assessment/Risk of Bias

The full texts were screened further for explicit of methodological descriptions of ADRs, drug therapy problems, geriatrics and the elderly. Studies were graded based on strong and weak recommendations of the study characteristics and quality to enhance critical appraisal.

Certainty Assessment

Publication bias, imprecision, inconsistency, and indirectness of evidence in the assessment were utilized for certainty of the study.

Data Collection

Literatures that reported the incidence of ADRs among Nigeria's geriatric population were reviewed. The databases utilized were Google Scholar, PubMed, and ResearchGate with no specific gate window. The references of some articles were also manually searched to identify more studies. The keywords "geriatric" [MeSH Terms], "adverse drug reaction" [MeSH Terms], "incidence" [MeSH Terms], "prevalence" [MeSH Terms], "older adults" [MeSH Terms], and "elderly" [MeSH Terms] were used. The free text included adverse drug reactions in the elderly in Nigeria and the incidence of adverse drug reactions in Nigeria. The selection was not restricted to a specific study design. However, the study was restricted to geriatric/elderly population for which the study could be generalized. Nonetheless, it is also possible that some studies may have been omitted due to this limitation and restricting the generalization.

The review concentrated on the prevalence, incidence, and challenges of adverse drug reactions in the elderly in Nigeria. Other age groups, however, were not overlooked. The literature and research on various elderly disease states were reviewed. Author, year of publication, age range, population size, study design, geopolitical zone, and most implicated medication were all extracted from the publications. Each conflict was discussed in the cases of disagreements until agreement was reached. The resulting data was kept open and detailed. Meta- analysis was not carried out because it is outside the scope of this study. Hence, heterogeneity was not assessed.

Data Synthesis

All the results of the primary studies were collated and summarized. A combination of descriptive synthesis with quantitative summary was utilized. The population, causes of ADR, comparisons, and outcomes were used as a framework. The study characteristics, causes of ADRs, and comparisons of implications and outcomes were tabulated in a spread sheet. Summary statistics of studies were also tabulated, while those without comprehensive summaries were excluded. Descriptive statistics was used to summarize the qualitative and quantitative data based on their homo- and heterogeneity. Sub-group analysis was used to explore heterogeneity. To assess the robustness of the synthesized result, range of values and alternatives were substituted for arbitrary and unclear decisions to ensure that decisions taken were rational and consistent.

Data Analysis

A descriptive analysis was performed to summarize the published articles. The studies and their characteristics were summarized based on the following: authors and year conducted, age range, setting/geographical zone, study design, prevalence, medications implicated, system, and organ most implicated in ADRs. The articles were evaluated for heterogeneities among the population group. Finally, an evidence-based table was synthesized.

Ethical Consideration

Published and freely available online literature and data on ADRs among geriatrics in Nigeria were reviewed online. Hence, ethical approval does not apply. This study was carried out strictly with the PRISMA-2020 Guideline for Systematic Reviews.

RESULTS & DISCUSSION

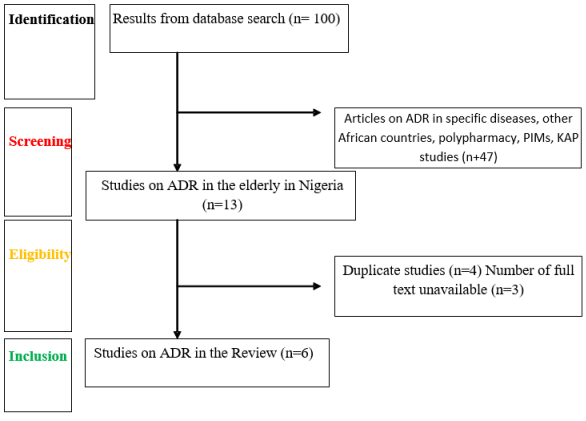


Figure 1: The PRISMA flow diagram for selection of articles

Out of the 100 reports initially identified, only thirteen reported adverse drug reactions in elderly patients in Nigeria. Articles that focused on adverse drug reactions in specific diseases, studies conducted in other African countries, studies on polypharmacy, potentially inappropriate medications (PIMs); and knowledge, attitude and practice (KAP) studies were excluded. Duplicate studies and studies without full texts available were also removed. Finally, six studies were included in the analysis.

Study Characteristics

Two of the six studies were conducted on the general adult population but provided specific information about older adults (Adedapo *et al.*, 2021; Akhideno *et al.*, 2018). All the studies were conducted among hospitalized patients, primarily in the Internal Medicine wards. The studies had a prospective, retrospective, or mixed design. The incidence of ADRs among elderly patients ranged from 6.2% to 31.1%. The gastrointestinal system was the most affected, and non-steroidal anti-inflammatory drugs (NSAIDs) were the most commonly implicated group of drugs causing ADRs. The majority of the studies were conducted in a single center (see Table 1). A summary of the factors responsible for ADRs in the included studies is shown in Table 2.

Table 1: Summary of studies on the incidence of ADRs among the elderly in Nigeria

Author (Year conducted)	Age Range	Population Size	Setting/ Geopolitical Zone	Study Design	Prevalence of ADRs	Three Most Implicated Medications	System/ Organ Most Implicated In ADR
Akhideno *et al.*, 2018 (2013-2014)	17-89 (adults) elderly as >64	507 (adults) 125 (elderly)	University of Benin Teaching Hospital, Benin City, Edo State/ South-South	Prospective study	4.4%	Insulin, NSAIDs and antihypertensives in adult population studied	Neurological. Gastrointestinal and dermatological systems
Amadi *et al.*, 2021	60 and above	126	University of Port-Harcourt Teaching Hospital, Port-Harcourt, Rivers State/ South-South	Cross-sectional sampling	19.8%	Chloroquine, Amlodipine	Integumentary/Skin, Central Nervous System, Gastrointestinal system
Saka *et al.*, (2017; 2018)	60 and above	268	Not Stated	Cross-sectional retrospective	13.8%	NSAIDs (Diclofenac), cardiovascular medications	Digestive system, vascular system, nervous system
Adedapo *et al.*, 2021 (2012-2013)	60 and above	1280 (total adult population) 418 (elderly population)	University College Hospital, Ibadan/ South-West	Prospective cohort study	4.9%	NSAIDs, hypoglycemic, antibacterial	Gastrointestinal, central nervous system, and skin/ cutaneous system

Nwani & Isah, 2017 (2009)	65 and above	345	Nnamdi Azikiwe University Teaching Hospital, Nnewi/ South-East	Prospective study	6.7%	NSAIDs, steroids, and hypoglycemic agents	Gastrointestinal system, central nervous system, endocrine and metabolic system
Eze *et al.*, 2011 (2008)	60 and above	375	Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State/South-West	Retrospective and prospective	31.1%	Cardiovascular medications	Not specified

Table 2: Summary of the factors responsible for ADRs in the included studies

Author (Year conducted)	Factors responsible for ADR
Akhideno *et al.*, 2018 (2013-2014)	Number of medications Number of co-morbidities
Amadi *et al.*, 2021	Polypharmacy Multi-morbidity Alcohol intake
Saka *et al.*, (2018; 2017)	Abrupt stoppage of medications Use of antiemetics Decreased potassium levels below 2.5mmol/L
Adedapo *et al.*, 2021 (2012-2013)	Outpatient medication errors Overdose Self-medication and drug misuse Multi-morbidity Duration of hospital stay Polypharmacy (≥3 medications)
Nwani & Isah, 2017 (2009)	Not reported
Eze *et al.*, 2011 (2008)	Polypharmacy (≥5 medications)

In one study on the general adult population (aged 17 years and older), elderly patients (65 and older) accounted for 24.7% of the study participants, and adverse drug reactions were observed in 22% of these elderly patients. Although the specific drug most implicated in elderly patients was not specified, the drugs most frequently associated with adverse drug reactions in the general adult population were insulin (27.5%), NSAIDs (19.6%), antihypertensives (15.7%), and antimalarials. Age was found to be a significant risk factor for adverse reactions to medications among the elderly, with those aged 65 years and older being at a higher risk than younger patients (Akhideno *et al.*, 2018).

A prospective cohort study was conducted, involving a total of 1,280 adult patients who were admitted to the hospital. It was found that patients aged 60 and older constituted approximately one-third (32.7%) of the study participants. Among patients aged 65 years and older, 4.9% experienced adverse drug reactions that resulted in hospitalization, while 1.3% developed adverse drug reactions during their admission. The study did not specify the most affected organ or system or the specific classes of drugs implicated in adverse drug reactions in the older population, but in the general adult population, the most implicated drug classes were NSAIDs, antidiabetics, and antibacterials. The gastrointestinal tract, central nervous

system, and skin were the organs and systems most commonly affected (Akhideno *et al*., 2018).

In a retrospective cross-sectional study of elderly patients, out of 268 admitted patients, 43 cases of adverse drug reactions (13.8%) were reported, with the digestive system being the most affected by these reactions. Only 9.3% of the total observed cases were formally documented as adverse drug reactions. The most implicated medication in these reactions was diclofenac (Saka *et al*., 2018).

Another study found that 19.8% of the elderly population experienced adverse drug reactions. The most common adverse reactions included itching (22%), drowsiness, dizziness, and restlessness. The drug most implicated in these reactions was chloroquine, and hypertension was a major medical ailment. It was observed that 96% of the patients had multiple morbidities, and 96% of those with adverse drug reactions were taking more than five drugs, compared to 86.14% of those without adverse drug reactions (Nwani & Isah, 2017).

Another prospective study evaluated 345 patients aged 65 years and older. Out of these patients, 23 (6.7%) experienced adverse drug reactions, with 73.9% of these cases recovering and 26.1% resulting in death. The most common adverse drug reaction observed was gastrointestinal bleeding (39.1%). The most implicated drug classes were NSAIDs, steroids, and hypoglycemic agents. The gastrointestinal system, central nervous system, and endocrine and metabolic systems were the organ systems most frequently involved. Adverse drug reactions were responsible for 1.7% of deaths among elderly patients who were admitted to the hospital (Nwani & Isah, 2017).

A study conducted by (Eze *et al*., 2011) focused on identifying drug therapy problems (DTPs) among elderly inpatients. The study utilized both retrospective and prospective methods. It reported that 31.1% of the total DTPs recorded was adverse drug reactions, but it did not provide further details on the drug classes responsible. However, cardiovascular medications were the therapeutic group most commonly associated with DTPs.

This present study evaluated the prevalence of adverse drug reactions among the elderly in Nigeria, and revealed a wide variation in the prevalence of ADRs. This variability may be due to factors such as differences in the methods used to identify an ADR, the sample size and study design. In this review, some of the studies relied on the identification of ADRs during routine hospital care or on self-reporting methods. However, this is prone to under-identification and under-reporting of ADRs, and such methods are likely to underestimate the true prevalence of ADRs (Kongkaew *et al*., 2008; Brvar *et al*., 2009; Ramia *et al*., 2021). These results are similar to the results of a systematic review of ADR in the elderly (Alhawassi *et al*., 2014).

NSAIDS are one of the most commonly used class of drugs for self-medication (Oriavwote & Ikwuka, 2022). NSAIDs are implicated in most of the ADRs and are the major causes of peptic ulcer diseases and worsening hypertensive conditions (Drini, 2017). Similar to (Kongkaew *et al*., 2008; Oscanoa *et al*., 2017; Hadia *et al*., 2022), NSAIDs and cardiovascular medications caused most ADRs in the elderly. However, (Jennings *et al*., 2020) reported diuretics and antibacterials for systemic use as the most implicated medications. Polypharmacy has also been shown by other systematic reviews conducted on the elderly as the major risk factor for ADRs in the elderly population (Davies *et al*., 2020; Hadia *et al*., 2022).

The incidence and prevalence of ADRs is under-reported in Nigeria, particularly among the geriatric population (Ogar *et al*., 2019). According to a study conducted in Nigeria, only 32% of health professionals report adverse drug reactions (Okezie & Olufunmilayo, 2008). Several reasons have been identified for the under-reporting of ADRs in Nigeria, including staff shortages, time required to assess and submit reports, lack of information, difficulties in diagnosing or identifying adverse reactions, ignorance of the importance of reporting, limited or no training for healthcare workers on ADR observation and reporting, lack of awareness of the reporting form, poor knowledge of the reporting procedure, and uncertainty of causality (Aderemi-Williams *et al*., 2015; Miediegha & Bunu, 2020; Okezie & Olufunmilayo, 2008; Oreagba *et al*., 2015).

The poor knowledge of healthcare professionals regarding ADRs is a cause for concern. In a study by (Adisa & Omitogun, 2019), only 15% of healthcare workers had adequate knowledge of ADRs. In another study, only 24.9% of respondents were aware of the national ADR reporting form (commonly known as the Yellow Form), and just 20.1% had received training in pharmacovigilance (Udoye *et al*., 2018).

Another challenge is developing policies and appointing staff who can understand and respond to the needs of the aging population. There are limited centers dedicated to the care of geriatric patients in Nigeria, resulting in inadequate attention to their specific needs before initiating treatment. Often, they are treated alongside adult patients under the age of 60. The prevalence of polypharmacy and the prescription of potentially inappropriate medications (PIMs) pose significant problems in the pharmacotherapy of older adults, leading to a significant increase in ADRs among the elderly. Studies conducted on the elderly in Nigeria have reported high rates of polypharmacy and PIMs, resulting in a high incidence of adverse drug reactions (Borodo *et al*., 2022).

The negative impact of adverse drug reactions on health outcomes in the geriatric population cannot be overstated. In developing countries like Nigeria, these effects are more pronounced due to high health outcome indicators. Older adults are more susceptible to ADRs compared to younger adults due to the increased risk associated with aging. It has been suggested that ADRs should be treated as a geriatric syndrome in themselves. The potential consequences of adverse drug reactions (ADRs) are multifaceted and include longer hospital stays, which in

turn increase morbidity and mortality rates, as well as healthcare costs (Fasipe *et al*., 2019).

Strategies must be put in place to reduce the incidence of ADRs (adverse drug reactions) among the elderly in Nigeria. One of the first steps in reducing the incidence of ADRs in Nigeria would be the proper reporting of cases. This would help to identify the particular classes of drugs responsible for adverse drug reactions in geriatrics, and strategies can be put in place to reduce their use or research safer pharmacological alternatives. A study in the United States among adults aged ≥65 years observed that three drug groups - medicines that help prevent blood clots, antidiabetic medications, and medications with morphine-like effects - were found to be involved in about 60% of Emergency Department visits for adverse drug reactions (Shehab *et al*., 2016).

The reporting of adverse drug reactions in Africa has been strengthened through the establishment of "National Pharmacovigilance Centers (NPCs)" in several countries (Ogar *et al*., 2019). The NPC in Nigeria has made available procedures for the proper reporting of ADRs (NPC, 2014). Furthermore, activities and programs such as public enlightenment and education of patients and caregivers on ADRs, as well as spontaneous reporting of ADRs by health professionals, should be implemented to increase the reporting rate.

The poor knowledge of ADRs among healthcare workers highlights the need for continuous mandatory education and training of health workers on adverse drug reactions and pharmacovigilance concepts. The curriculum of health professionals during undergraduate training should also emphasize the identification, prevention, and documentation of adverse drug reactions. To tackle the problem of limited centers dedicated to the care of geriatric patients, the leadership of various hospitals and clinics should advocate for the establishment of geriatric centers in their facilities equipped with trained staff across all states in Nigeria.

Reducing pill burden, referred to as deprescribing, is one of the most effective steps to reducing adverse drug reactions among the elderly. Deprescribing refers to the process of withholding unnecessary medicines or minimizing their dosages at the discretion of a healthcare professional, probably a medical doctor or a pharmacist. This is aimed at managing polypharmacy and in turn, improving health outcomes. There should be an increase in awareness among Nigerian prescribers regarding rational prescribing (Oli *et al*., 2021) and the use of checklists (or Trigger Tools) for ADR detection among the elderly (Borodo *et al*., 2022).

Reports on the incidence of adverse drug reactions in the geriatric population in Nigeria are very limited. Thus far, only two reports are documented solely on ADRs in geriatrics in Nigeria. Most studies are focused on ADRs in the general adult population and potentially inappropriate prescribing. However, high quality reports investigating the drug classes most responsible for ADRs in the elderly are lacking. Furthermore, interventions to reduce ADRs and improve healthcare among geriatric patients in Nigeria are limited.

This present study is not without limitations as it utilized heterogeneous studies (prospective, retrospective, and mixed) in the review and this poses a bias. Although retrospective studies have been shown to detect lower ADRs compared to prospective studies because they are subject to failure in gathering and proper documentation of data in the medical charts (De Figueiredo *et al*., 2017), however, this was not so in this present study as those that used a prospective study design had lower ADR prevalence rates compared to those with a retrospective design. Another limitation of this present study is the variation in the age brackets of the elderly patients included in the review. There is a need for further studies on the detection of ADRs and trigger tools/medications that cause a significant burden of morbidity and mortality in Nigeria's geriatric population.

CONCLUSION

The geriatrics are highly susceptible to adverse drug reactions due to the decline in cellular functions, co-morbid conditions, and polypharmacy. These factors contribute to increased risk of hospitalizations and deaths resulting from medication-related adverse events. Despite the high risks involved, approaches to addressing ADRs have not focused solely on the geriatric population. Interventional studies on safer non-pharmacological and pharmacological alternatives to drug classes associated with ADRs are necessary in order to reduce the occurrence of ADRs among the geriatric population in Nigeria.

Acknowledgments

Special thanks to everyone who contributed in one way or the other to make this research a success. Your assistance in conducting this research is highly appreciated.

REFERENCES

Adedapo, A. D., Adedeji, W. A., Adedapo, I. A., & Adedapo, K. S. (2021). Cohort study on adverse drug reactions in adults admitted to the medical wards of a tertiary hospital in Nigeria: Prevalence, incidence, risk factors and fatality. *British Journal of Clinical Pharmacology, 87*(4), 1878-1889. https://doi.org/10.1111/bcp.14577.

Aderemi-Williams, R., Awodele, O., & Boyle, C. (2015). Adverse drug reactions amongst adult patients admitted in Lagos State University Teaching Hospital Lagos, Nigeria. *Current Drug Safety, 10*(2), 136-144. https://doi.org/10.2174/1574886309666140601211211.

Adisa, R., & 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*, 1-14. https://doi.org/10.1186/s12913-019-4775-9.

Akhideno, P. E., Fasipe, O. J., & Isah, A. O. (2018). The

incidence and prevalence of adverse drug reactions among medical inpatients in a Nigerian University Teaching Hospital. *Journal of Current Research in Scientific Medicine, 4*(2), 86-93.

Alhawassi, T. M., Krass, I., Bajorek, B. V., & Pont, L. G. (2014). A systematic review of the prevalence and risk factors for adverse drug reactions in the elderly in the acute care setting. *Clinical Interventions in Aging, 9,* 2079-2086. https://doi.org/10.2147/CIA.S71178.

Ama, M. I., Ikwuka, A. O., Udeh, F. C., Ekechi, H. O., & Eteudo, A. N. (2023). Sperm Parameters and Testicular Histology of Male Wistar Rats Treated with Phoenix dactylifera After Consumption of Local Mmahi Salt. *American Journal of Bioscience and Bioinformatics, 2*(1), 41-51. https://doi.org/10.54536/ajbb.v2i1.2275.

Amadi, E. S., Pepple, E. F., Otike-Odibi, B., & Bell-Gam, H. I. (2021). Adverse drug reactions amongst admitted advanced age Africans. *World Journal of Advanced Research and Reviews, 12*(3), 427-433. https://doi.org/10.30574/wjarr.2021.12.3.0712.

Aronson, J. K., & Ferner, R. E. (2005). Clarification of terminology in drug safety. *Drug Safety, 28*, 851-870.

Baysah, P. V., Ikwuka, A. O., Udeh, F. C., Bleh, D. P., & Viloria, T. (2023). Pathophysiological effects of alcohol and tobacco consumption on semen parameters of men attending a fertility clinic in West Africa. *American Journal of Biomedical and Life Sciences, 11*(4), 73-81. https://doi.org/10.11648/j.ajbls.20231104.13.

Borodo, S. B., Jatau, A. I., Mohammed, M., Aminu, N., Shitu, Z., & Sha'aban, A. (2022). The burden of polypharmacy and potentially inappropriate medication in Nigeria: a clarion call for deprescribing practice. B*ulletin of the National Research Centre, 46*(1), 1-8. https://doi.org/10.1186/s42269-022-00864-3.

Brvar, M., Fokter, N., Bunc, M., & Mozina, M. (2009). The frequency of adverse drug reaction related admissions according to method of detection, admission urgency and medical department specialty. *BMC Clinical Pharmacology, 9*, 1-8.

Charlesworth, C. J., Smit, E., Lee, D. S., Alramadhan, F., & Odden, M. C. (2015). Polypharmacy among adults aged 65 years and older in the United States: 1988–2010. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences, 70*(8), 989-995. https://doi.org/10.1093/gerona/glv013.

Cohen, J. (1968). Weighted kappa: nominal scale agreement provision for scaled disagreement or partial credit. *Psychological Bulletin, 70*(4), 213. https://doi.org/10.1037/h0026256.

Coleman, J. J., & Pontefract, S. K. (2016). Adverse drug reactions. *Clinical Medicine, 16*(5), 481. https://doi.org/10.7861/clinmedicine.16-5-481.

Davies, E. A., & O'mahony, M. S. (2015). Adverse drug reactions in special populations–the elderly. *British Journal of Clinical Pharmacology, 80*(4), 796-807. https://doi.org/10.1111/bcp.12596.

Davies, L. E., Spiers, G., Kingston, A., Todd, A., Adamson, J., & Hanratty, B. (2020). Adverse outcomes of polypharmacy in older people: systematic review of reviews. *Journal of the American Medical Directors Association, 21*(2), 181-187.

de Figueiredo, T. P., de Souza Groia, R. C., Barroso, S. C. C., do Nascimento, M. M. G., & Reis, A. M. M. (2017). Factors associated with adverse drug reactions in older inpatients in teaching hospital. *International Journal of Clinical Pharmacy, 39*, 679-685.

Drini M. (2017). Peptic ulcer disease and non-steroidal anti-inflammatory drugs. *Aust Prescr, 40*(3), 91-93. https://doi.org/10.18773/austprescr.2017.037.

Ekechi, H. O., Ikwuka, A. O., Udeh, F. C., & Abraham, J. C. (2023a). Effects of Ethanol Extract of Rauwolfia vomitoria Leaf on Lipid Profile and Cerebellar Histology in Cisplatin-induced Oxidative Stress. *British Journal of Medical and Health Research, 10*(5), 16-39. https://doi.org/10.5281/zenodo.8042521.

Ekechi, H. O., Ikwuka, A. O., Udeh, F. C., Epete, M. A., & Uche, V. U. (2023)b. Hepatorenal Protective Functions of Coconut Water in Alloxan-Induced Type 1 Diabetes Mellitus. *World Journal of Current Medical and Pharmaceutical Research, 5*(4), 114-122. https://doi.org/10.37022/wjcmpr.v5i4.276.

Eze, U. I. H., Oparah, C. A., & Lawal, F. A. (2011). Identification of Drug Therapy Problems among Elderly in-patients of a Nigerian Teaching Hospital. *Nigerian Journal of Pharmaceutical Research, 9*(1), 49-56.

Fasipe, O. J., Akhideno, P. E., & Owhin, O. S. (2019). The observed effect of adverse drug reactions on the length of hospital stay among medical inpatients in a Nigerian University Teaching Hospital. *Toxicology Research and Application, 3*, 2397847319850451. https://doi.org/10.1177/2397847319850451.

Hadia, R., Joshi, D., Bhil, D., & Maheshwari, R. (2022). Incidence of adverse drug reactions among elderly patients: A systematic review and meta-analysis. *Journal of the Scientific Society, 49*(2), 91-102.

Ikwuka, A. O. (2015). *Risk factors for the pathogenesis of diabetes mellitus type 2. Materials of 84th Scientific and Practical Conference of Students and Young Scientists with International Participation "Innovations in medicine"*, p. 19. Available online: http://www.ifnmu.edu.ua/images/snt/files/konferenciya/Tezu_2015.pdf

Ikwuka, A. O. (2017a). Dyslipidemia risk severity in patients with diabetes mellitus type 2 and essential hypertension. *Journal of the 21st International Medical Congress of Students and Young Scientists*, p. 59.

Ikwuka, A. O. (2017b). Effectiveness of dapagliflozin in patients with diabetes mellitus type 2 and essential hypertension. Book of abstracts of the *7th International Students' Scientific Conference of Young Medical Researchers*, p. 102. Available online: http://www.stn.umed.wroc.pl/files/lm/Accepted_papers.16113.pdf

Ikwuka, A. O. (2017c). Influence of dyslipidemia in patients with diabetes mellitus type 2 and essential hypertension. *The Pharma Innovation Journal, 6*(3), 101-103. Available online: http://www.thepharmajournal.

com/archives/?year=2017&vol=6&issue=3&part=B

Ikwuka, A. O., & Haman, I. O. (2017d). Features of kidney damage in patients with diabetes mellitus type 2 and essential hypertension. Journal of *86th Scientific and Practical Conference of Students and Young Scientists with International Participation "Innovations in medicine"*, p. 144. Available online: http://www.ifnmu.edu.ua/images/snt/86-konf-tezi%20(1).pdf

Ikwuka, A. O., Virstyuk, N. G., & Luchko, O. R. (2017)e. Features of the functional state of kidneys in patients with diabetes mellitus type 2 and essential arterial hypertension. *Materials of scientific-practical conference with international participation "Babenkivski reading"*, p. 48.

Ikwuka, A. O. (2018a). Clinical dynamics in patients with diabetes mellitus type 2 and concomitant essential hypertensive disease treated with dapagliflozin. *Journal of the 22nd International Medical Congress of Students and Young Scientists,* p. 32.

Ikwuka, A. O. (2018b). Clinical effectiveness of SGLT-2 inhibitors in patients with diabetes mellitus type 2 and essential hypertensive disease. *Endocrine Practice, 24*(1), 74. https://doi.org/10.1016/S1530-891X(20)47129-0.

Ikwuka, A. O. (2018c). Features of kidney damage in patients with arterial hypertension and type 2 diabetes mellitus and optimization of treatment. *Specialized Academic Council IFNMU*, Available online: http://www.ifnmu.edu.ua/images/zagalna_informacia/spec_vcheni_radi/2017-2019/%D0%9420.601.01/Ikvuka/Avtoreferat.pdf

Ikwuka, A. O., & Paliy, Yu. (2018d). Structural changes of the left ventricular myocardium in patients with essential arterial hypertension and diabetes mellitus type 2. Abstracts of the *87th Scientific Conference of Students and Young Scientists with International Participation "Innovations in medicine"*, p. 25-26. Available online: https://www.ifnmu.edu.ua/images/snt/zaproshennia_eng.pdf

Ikwuka, A. O. (2019a). Clinical dynamics of nephropathy in patients with diabetes mellitus type 2 and concomitant essential hypertensive disease. *Clinical Medicine, 19*(2), s39. https://doi.org/10.7861/clinmedicine.19-2-s39.

Ikwuka, A. O. (2019b). Clinical effectiveness of GLP-1 RAs in patients with metabolic syndrome diseases. *Endocrine Practice, 25*(1), 104-105. https://doi.org/10.1016/S1530-891X(20)46611-X.

Ikwuka, A. O., & Virstyuk, N. G. (2019c). Pattern of cardiac remodelling of the left ventricle in patients with essential hypertensive disease and concomitant type 2 diabetes mellitus. *Clinical Medicine, 19*(3), s92. https://doi.org/10.7861/clinmedicine.19-3-s92.

Ikwuka, A. O., & Virstyuk, N. G. (2021). Influence of SGLT2 inhibitor and A2RB (AT1) on fibrogenesis and heart failure in patients with essential hypertensive disease combined with diabetes mellitus type 2. E-Poster No. 143 of the *44th & 45th Annual General and Scientific Meeting of the West African College of Physicians (WACP)*, 1 - 3 November, 2021. https://doi.org/ 10.13140/RG.2.2.26912.87047.

Ikwuka, A. O., & Virstyuk, N. (2022). Prognostic markers of nephropathy in patients with dual metabolic syndrome diseases (essential hypertensive disease and concomitant type 2 diabetes mellitus). *Endocrine Practice, 28*(5), S65-S66. https://doi.org/10.1016/j.eprac.2022.03.164.

Ikwuka, A. O. (2023a). D*r. Aloy's Core Essential Series (DACES) Medical Genetics*. 1st Edition. Science and Education Publishing, USA, p. 9-10. ISBN: 978-1-958293-02-7.

Ikwuka, A. O. (2023b). *Dr. Aloy's Core Essential Series (DACES) Immunology*. 1st Edition. Science and Education Publishing, USA, p. 48. ISBN: 978-978-795-866-7.

Ikwuka, A. O., & Virstyuk, N. (2023c). Patterns and Influence of Cardio-Metabolic Insufficiency in Patients with Essential Hypertensive Disease and Concomitant Type 2 Diabetes Mellitus. https://doi.org/(5), S32-S33. https://doi.org/10.1016/j.eprac.2023.03.076.

Ikwuka, A. O., Virstyuk, N. G., Luchko, O. R., & Kobitovych, I. (2023d). Heterogeneity Of Renal Pathogenicity On The Background Of Asymptomatic Hyperuricemia In Patients With Dual Metabolic Syndrome Diseases (Essential Hypertensive Disease and Type 2 Diabetes Mellitus). *British Journal of Medical and Health Research, 10*(2), 1-9. https://doi.org/10.5281/zenodo.7690636.

Ikwuka, A. O. (2023e). *Dr. Aloy's Core Essential Series (DACES) Hematology*. 1st Edition. Science and Education Publishing, USA, p. 47-60. ISBN: 978-1-958293-09-6.

Ikwuka, A. O., Omoju, D. I., & Mahanera, O. K. (2023) f. Profiling of Clinical Dynamics of Type 2 Diabetes Mellitus in Patients: A Perspective Review. *World Journal of Current Medical and Pharmaceutical Research, 5*(5), 210-218. https://doi.org/10.37022/wjcmpr.v5i5.294.

Ikwuka, A. O., Virstyuk, N., Luchko, O., & Kobitovych, I. (2024). Optimization of treatment in MSD patients using a combination of HMG-CoA reductase inhibitor, SGLT-2 inhibitor and A2RB (AT1): Resultant clinical effectiveness. *Endocrine Practice, 30*(5), S60-S61. https://doi.org/10.1016/j.eprac.2024.03.243.

Inya, A. U., Achara, A. P., Ikwuka, A. O., Udeh, F. C., Chi-kadibia, U., & Onazi, O. (2023a). Clinical Dynamics of Anemia in Pregnancy: A 16-week Cross-sectional Study of Pregnant Women Who Attended Antenatal Clinic of Federal Medical Center, Keffi, Nasarawa State, Nigeria. *American Journal of Clinical Medicine Research, 11*(1), 1-9. https://doi.org/10.12691/ajcmr-11-1-1.

Inya, A. U., Achara, A. P., Ikwuka, A. O., Udeh, F. C., Chi-kadibia, U., & Onazi, O. (2023b). Patterns, Peculiarities and Associated Risk Factors of Anemia

in Pregnancy: A Case Study of Pregnant Women Attending Antenatal Clinic in North-Central Nigeria. *European Journal of Preventive Medicine, 11*(2), 21-31. https://doi.org/10.11648/j.ejpm.20231102.12.

Jaspinder, K., Sargun, S., & Kawaljit, K. (2014). Impact of age on the prevalence of chronic diseases in geriatric population. *International Research Journal of Biological Sciences, 3*(9), 79-85.

Jennings, E. L., Murphy, K. D., Gallagher, P., & O'Mahony, D. (2020). In-hospital adverse drug reactions in older adults; prevalence, presentation and associated drugs—a systematic review and meta-analysis. *Age and Ageing, 49*(6), 948-958.

Kongkaew, C., Noyce, P. R., & Ashcroft, D. M. (2008). Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. *Annals of Pharmacotherapy, 42*(7-8), 1017-1025.

Mekonnen, A. B., Alhawassi, T. M., McLachlan, A. J., & Brien, J. A. E. (2018). Adverse drug events and medication errors in African hospitals: a systematic review. *Drugs - Real World Outcomes, 5*, 1-24. https://doi.org/ 10.1007/s40801-017-0125-6

Miediegha, O., & Bunu, S. J. (2020). Pharmacovigilance framework and extent of medications adverse reaction surveillance in Southern Nigeria. *World Journal of Pharmaceutical Research, 9*(6), 2009-2017. https://doi.org/10.20959/wjpr20206-17727.

Musa, S., Ikwuka, A. O., Udeh, F. C., Musa, A. A., & Chukwuezie, U. C. (2023). CRISPR-Cas9 Genomic Editing as an Innovation in the Management of Sickle Cell Disease: A Systematic Review. *American Journal of Medical Science and Innovation, 2*(2), 36-48. https://doi.org/10.54536/ajmsi.v2i2.1760.

National Pharmacovigilance Center (NPC), Nigeria. (2014). *Guide for Reporting Adverse Reactions to Marketed Drugs.* Available online: http://www.rrfa.co.za/wp-content/uploads/2014/01/PV-Guideline-received-2012.pdf

Nwani, P. O., & Isah, A. O. (2017). Frequency and patterns of adverse drug reactions among elderly in-patients in a Nigerian teaching hospital. *J Basic Clin Pharm, 8*, 245-250.

Ogar, C. K., Abiola, A., Yuah, D., Ibrahim, A., Oreagba, I. A., Amadi, E. C.. & Oshikoya, K. A. (2019). A retrospective review of serious adverse drug reaction reports in the Nigerian VigiFlow database from September 2004 to December 2016. *Pharmaceutical Medicine, 33*, 145-157. https://doi.org/10.1007/s40290-019-00267-2.

Okezie, E. O., & Olufunmilayo, F. (2008). Adverse drug reactions reporting by physicians in Ibadan, Nigeria. *Pharmacoepidemiology and Drug Safety, 17*(5), 517-522. https://doi.org/10.1002/pds.1597.

Oli, A. N., Onyeaso, N., Emencheta, S. C., Ofomata, C. M., Kretchy, J. P., Okhamafe, A., & Ele, G. N. (2021). Evaluating antimicrobial prescribing in a Tertiary Healthcare Institution in Nigeria. *Journal of Pharmaceutical Policy and Practice, 14*(1), 1-6.

Oreagba, I. A., Bada, S. O., & Chuka-Ebene, V. (2015). An intensive study of adverse events in the Medical Unit of a Nigerian Teaching Hospital. *Value in Health, 18*(3), A86-A87. https://doi.org/10.1016/j.jval.2015.03.506

Oriavwote, P. E., & Ikwuka, A. O. (2022). Patterns and factors influencing self-medication among students of the American International University West Africa (AIUWA), The Gambia. *European Journal of Clinical Medicine, 3*(2), 33-37. https://doi.org/10.24018/clinicmed.2022.3.2.181.

Oscanoa, T. J., Lizaraso, F., & Carvajal, A. (2017). Hospital admissions due to adverse drug reactions in the elderly: A meta-analysis. *European Journal of Clinical Pharmacology, 73*, 759-770.

Prince, M. J., Wu, F., Guo, Y., Robledo, L. M. G., O'Donnell, M., Sullivan, R., & Yusuf, S. (2015). The burden of disease in older people and implications for health policy and practice. *The Lancet, 385*(9967), 549-562. https://doi.org/10.1016/S0140-6736(14)61347-7.

Ramia, E., Zeenny, R. M., Hallit, S., & Salameh, P. (2021). A population-based study of self-reported adverse drug events among Lebanese outpatients. *Scientific Reports, 11*(1), 7921.

Saka, S. A., Nlooto, M., & Oosthuizen, F. (2018). American Geriatrics Society-Beers Criteria and adverse drug reactions: a comparative cross-sectional study of Nigerian and South African older inpatients. *Clinical Interventions in Aging, 13*, 2375-2387. https://doi.org/10.2147/CIA.S176899.

Saka, S. A., Oosthuizen, F., & Nlooto, M. (2017). Interventions towards reducing adverse drug reactions among geriatric population in Africa: a scoping review of the literature from 1990–2016. *PULA: Botswana Journal of African Studies, 31*(1), 180-194.

Shehab, N., Lovegrove, M. C., Geller, A. I., Rose, K. O., Weidle, N. J., & Budnitz, D. S. (2016). US emergency department visits for outpatient adverse drug events, 2013-2014. *JAMA, 316*(20), 2115-2125. https://doi.org/ 10.1001/jama.2016.16201.

Uche, V. U., Ikwuka, A. O., Udeh, F. C., Okorocha, A. E., Epete, M. A., Ekechi, H. O., Abraham, J. C., & Igwe, E. C. (2023). Associated Risks and Pathogenic Effects of Consumption of Calcium Carbide-Ripened Banana Before and/or During Pregnancy on Maternal and Neonatal Livers. *American Journal of Food Science and Technology, 2*(2), 54-64. https://doi.org/10.54536/ajfst.v2i2.2197.

Udoye, J. A., Ozolua, R. I., & Nwokike, J. (2018). Assessment of the knowledge, attitude and practice of pharmacovigilance by pharmacists in two states in southeastern Nigeria. *Tropical Journal of Pharmaceutical Research, 17*(5), 937-945. https://doi.org/10.4314/tjpr.v17i5.25.

Virstyuk, N. G., Ikwuka, A. O., Haman, I. O., & Adebomi, M. S. (2016). Diabetes mellitus type 2, arterial

hypertension and dyslipidemia. Materials of *2nd International Scientific and Practical Conference "Therapeutic readings: modern aspects of diagnosis and treatment of diseases of internal organs"*, p. 46-47.

Virstyuk, N. G., & Ikwuka, A. O. (2017a). Diagnostic and prognostic markers of the diabetes mellitus type 2 course in connection with essential arterial hypertension taking into account the kidney function. *Precarpathian Journal Pulse, 8*(44), 53-62.

Virstyuk, N. H., Ikwuka, A. O., Losyuk, L. V., Kobrynska, O. Ya., & Markiv, H. D. (2017b). Dapagliflozin utility in patients with diabetes mellitus type 2 and essential hypertensive disease. *Actual Problems of Modern Medicine, 4*(60)1, 76-79. Available online: http://www.umsa.edu.ua/journal2stat4_2017_eng.html

Virstyuk, N. G., & Ikwuka, A. O. (2018a). Features of asymptomatic hyperuricemia in patients with diabetes mellitus type 2 and concomitant essential arterial hypertension. *Clinical and Experimental Pathology, 1*(63), 22-26. https://doi.org/10.24061/1727-4338.XVII.1.63.2018.5.

Virstyuk, N. G., Ikwuka, A. O., & Didushko, O. M. (2018b). Effect of dapagliflozin on the level of uric acid during asymptomatic hyperuricemia in patients with diabetes mellitus type 2 and concomitant arterial hypertension. *Art of Medicine, 1*(5), 21-26. Available online: https://art-of-medicine.ifnmu.edu.ua/index.php/aom/article/view/179/150

Virstyuk, N. H., & Ikwuka, A. O. (2018c). Dapagliflozin influence on the clinical course of diabetes mellitus type 2 and essential hypertension in patients. Recent Advances in Environmental Science from the Euro-Mediterranean and Surrounding Regions, p. 2007-2008. https://doi.org/10.1007/978-3-319-70548-4_582.

Virstyuk, N. G., & Ikwuka, A. O. (2019). Nephropathic characteristics in patients with diabetes mellitus type 2 and essential hypertensive disease. Art of Medicine, 1(5), 44-47. https://doi.org/10.21802/artm.2019.1.9.44.

Virstyuk, N. G., & Ikwuka, A. O. (2021a). Asymptomatic hyperuricemia and functional state of the kidneys in patients with essential arterial hypertension and concomitant diabetes mellitus type 2. *European Journal of Clinical Medicine, 2*(3), 100-104. https://doi.org/10.24018/clinicmed.2021.2.3.65.

Virstyuk, N. H., Ikwuka, A. O., Luchko, O. R., & Kocherzhat, O. I. (2021b). Peculiarities of renal insufficiency in patients with diabetes mellitus type 2 and arterial hypertension. *Materials of scientific-practical conference with international participation "Achievements and prospects of experimental and clinical endocrinology" Twentieth Danilevsky readings*, p. 86-87.

World Health Organization (WHO). (2019). *Medication Safety in Polypharmacy.* (WHO/UHC/SDS/2019.11). Available online: https://www.who.int/docs/default-source/patient-safety/who-uhc-sds-2019-11-eng.pdf

Yadesa, T. M., Kitutu, F. E., Deyno, S., Ogwang, P. E., Tamukong, R., & Alele, P. E. (2021). Prevalence, characteristics and predicting risk factors of adverse drug reactions among hospitalized older adults: A systematic review and meta-analysis. *SAGE Open Medicine, 9*, 20503121211039099. https://doi.org/10.1177/20503121211039099.

Zazzara, M. B., Palmer, K., Vetrano, D. L., Carfì, A., & Graziano, O. (2021). Adverse drug reactions in older adults: a narrative review of the literature. *European Geriatric Medicine, 12*, 463-473. https://doi.org/10.1007/s41999-021-00481-9.