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IDENTIFICATION OF POTENTIALLY INAPPROPRIATE MEDICATIONS USING EXPLICIT CRITERIA AMONG GERIATRIC PATIENTS IN A NIGERIAN SPECIALIST HOSPITAL

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ABSTRACT
Introduction: Potentially inappropriate medications [PIM] are a common cause of morbidity and mortality among the elderly. Detection and prevention of inappropriate medication should be a major concern of prescribers and pharmacists. Several assessment tools are available for detection of PIMs and each one of them have their own limitations. Literature reports reveal wide variations using different tools which makes comparism rather difficult. It is important that PIMs are avoided by using appropriate setting specific tool(s) so as to reduce risk of drug misadventure. **Aim**: To determine drug prescription pattern and assess prevalence of PIMs. **Method**: It is cross sectional retrospective study using medication records of geriatric patients attending a Specialist hospital. A total of 500 medical records were selected by simple random sampling method and relevant data extracted for analysis. **Result/Discussion**: The result showed PIM prevalence is high compared to previous studies. Assessment of PIM produced overall prevalence of 56.1 % most of which were associated with non-steroidal anti-inflammatory analgesics, Benzodiazepines and antidiabetics. The assessment tools produced varying prevalence rates which suggest that no one tool will be effective in detecting all PIMs. **Conclusion**: The prevalence of PIMs is high, so there is need to improve detection of inappropriate medications in geriatrics in order to prevent adverse drug events.

KEYWORDS: Geriatrics, Potentially inappropriate medications, assessment tools.

INTRODUCTION
The elderly population is growing globally occasioned by improvements in the standard of living and good healthcare services. The World Health Organization defines the population of ≥ 65 years as elderly; these groups of patients often require regular medical care and sometimes expensive therapies. As life expectancy rises globally there is a corresponding increase in incidence of multi-morbidities among geriatric population.[1,2,3] The ageing process is highly variable and significant differences exist in the extent to which ageing impact on individuals' health, functional independence and drug handling.

There is ample evidence that ageing significantly affects pharmacokinetics and pharmacodynamic properties of drugs, which exposes the elderly to higher risk of adverse drug reactions and mortality. There is also increased frequency and length of hospitalizations related to adverse drug reactions with associated high cost of medical care.[4,5,6,7] The increased risk of adverse drug reactions is primarily due to frailty, comorbidity of chronic diseases and decreased physiologic organ reserve.[8,9] The elderly often require multiple medications thus making polypharmacy inevitable with its attendant potential for adverse events. It is estimated that between 12 – 23% of elderly patients older than 65 years are taking up to 10 drugs at any given time[10,11], though similar studies reported between 2 – 5 medications.[12,13] The variations stem largely from differences in characteristics of geriatric population studied, disease pattern and healthcare systems. Polypharmacy and the use of non-prescription medications among the elderly equally carry significant risk of preventable morbidity, mortality, cognitive decline and diminished quality of life.[14,15]

Medication related morbidity arising from medications is preventable if structural and administrative processes ensure that mediation errors are detected early.[16,17] Prevalence of potentially inappropriate medications [PIM] varies widely depending on study settings and

tools of assessment, however there have been consistent reports that prevalence is high. Some studies reported that above 50% of elderly patients encounter potentially inappropriate medicine [PIM].[11,18] Several studies estimated PIM prevalence of between 21 -29% and its often associated with increased risk of mortality, physical and functional decline as well as difficulties with basic self-care.[19,20] Inappropriate medication is an independent predictor of long term mortality among the elderly.[21] It has been estimated that elderly patients with PIM is about twice more likely to experience an adverse drug reaction.[22] Some studies reported that over 50% of hospital admissions among the elderly are related to adverse drug reactions occasioned by PIM.[23,24]

Polypharmacy is an important risk factor for increased length of hospital admission and rehospitalization.[25,26] There is significant correlation between polypharmacy and inappropriate medications.[27,28,29,30,31,32] Medication errors not only affect achievement of treatment outcomes but also cause higher rates of hospitalization and mortality among the elderly.[33,34]

The need to detect and prevent potentially inappropriate medications led to the development of several tools that have found application in healthcare and research.[35] These tools which may be based on explicit or implicit criteria were largely developed by consensus opinion of experts using Delphi method. The most widely used of these tools is the Beers criteria; in-spite of its many limitations in identifying drug – drug interactions, duplicate class prescription and under prescription, it remains a useful tool in identification of PIMs.[36,37,38] Other explicit criteria based tools for detecting PIM include "Improved prescribing in the elderly tool "IPET".[39], Prescribing appropriateness index "PAI"[40], Zhans criteria[41], French consensus panel list, "STOPP/START"[42], Australian prescribing indicators tool[43], Norwegian general practice "NORGEP"[44], "PRISCUS" list[45], Thailand criteria[46], Assessing care of vulnerable elders "ACOVE" tool[47], Rancourt criteria[48] and Bergen district nursing home tool "BEDNURS".[49]

A number of tools based on specific quality indicators are not disease specific, so require application of professional judgment to determine appropriateness. Among these implicit criteria based tools are medication appropriateness index MAI[50,51] and assessment of under-utilization of medication tool AOU.[52]

There is no single tool that meets all criteria for drug safety, so in practice a combination of tools may be used depending on setting and instrument reliability. The improvement of medication safety in the elderly is an ongoing effort; one of these is multidisciplinary team of healthcare professionals who make comprehensive evaluation of physical and medical care needs and then agree on the most appropriate medication(s). This approach has shown promising results across all domains of appropriateness.[53] Other innovations involves prescriber education, audit and feedback and computerized provider order entry with clinical decision support all of which are promising with regards to improvement in prescribing habits.[54,55,56,57]

OBJECTIVES

- To determine drug prescription pattern among the elderly
- To compare prevalence of PIM using different assessment tools

METHODS

Setting: The study was carried out in the outpatient department of Borno State specialist hospital Maiduguri, North east Nigeria. It is a cross sectional retrospective study involving elderly patient's ≥ 65 years who had and/or are receiving medical care in the hospital between January 2016 and June 2018.

SAMPLING: A total of 966 elderly patients attending the hospital were eligible for inclusion in the study. Patients with incomplete medical and prescription records or become deceased within the period were excluded.

DATA COLLECTION: Data obtained from the medical records of the patients include demographic information, diagnosis, morbidities, prescribed drugs, dosages and duration of treatment. Potentially inappropriate medications were determined by comparing prescribed drugs with those listed in these seven explicit criteria [Beers criteria 2012, STOPP/START, NORGEP criteria, BEDNURS criteria, PRISCUS list, French consensus panel list and Rancourt criteria]. If the prescribed drug or drug combination is found in any of the criteria, it is noted as inappropriate medication. For the purpose of calculating prevalence each inappropriate medication is counted as one even if it appears multiple times in prescriptions.

ANALYSIS: The data were analyzed using six explicit criteria. The prescriptions were reviewed for the presence of PIM in each of the six explicit criteria. Each prescription is reviewed and compared with the list of PIM, drug combinations and interactions with other drugs and diseases. Where evidence of inappropriate medication, combinations or interactions exists it is noted as PIM under the assessment tool.

Ethical approval: This was obtained from the human research ethics committee of Borno State Specialist hospital, Maiduguri.

RESULTS

The average age was 75.2 years and females constitute more than three quarter of patients. Majority were on treatment for one chronic disease and on an average of 6.4 drugs. More than half of them have been exposed one or more potentially inappropriate medication with an average of 1.8 PIM per patient.

TABLE 1: DEMOGRAPHIC DATA [N = 966]

AGE [yrs.]	
65 – 69	107[11.1%]
70 – 74	242[25.1%]
75 – 79	496[51.3%]
≥ 80	121[12.5%]
Mean Age [yrs.]	75.2±14.5
GENDER [n = 966]	
Male	246 [25.5%]
Females	720 [74.5%]
MORBIDITY [n = 966]	
1	845[87.5%]
2	113[11.7%]
3	8[0.8%]
NUMBER OF DRUG PRESCRIPTIONS [n = 2216]	
1 – 3	242[10.9%]
4 – 6	728[32.9]
≥7	1246[56.2]
MEAN DRUGS PER PRESCRIPTION	6.4±2.5
TOTAL NUMBER OF PIMS	**542 [56.2%]**
PIM/PATIENT [n = 966]	
1	377[39.0%]
2	110[11.4%]
3	55[5.7%]
Average PIM per patient = 1.8	

The most prescribed class of drugs are the antihypertensives [71.3%] followed by analgesics and antibiotics. The other classes of drugs frequently prescribed ranged from 1 – 20%.

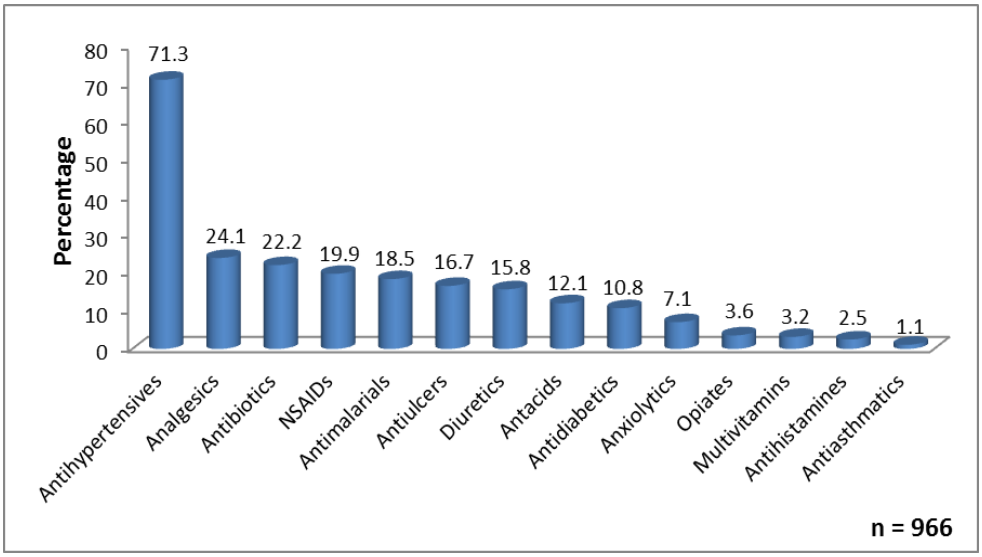


FIG 1: CLASS OF DRUGS PRESCRIBED.

Evaluation of prescriptions showed that BENADURS, NORGEP and Beers criteria produced PIM prevalence of 73.2%, 33.4% and 32.4% respectively. Other assessment tools like STOPP/START and PRISCUS list produced PIM prevalence of about 27.2 and 27.9% respectively. The overall PIM prevalence rate using six criteria ranged between 22 – 73% of all the prescriptions.

TABLE 2: POTENTIALLY INAPPROPRIATE MEDICATION USING SIX EXPLICIT CRITERIA.

Name of drug [n = 930]	N	Beers criteria	STOP/ START	NORGEP Criteria	BENDNURS criteria	PRISCUS List	French consensus Panel list
Digoxin 250mcg	5	+	+	--	--	+	--
Methyldopa	3	+	--	+	--	+	+
Chlorpheniramine	32	+	+	+	--	+	+
Diphenhydramine	15	+	+	+	--	+	+
Promethazine	15	+	+	+	--	+	+
Hyoscine	25	+	+	--	--	--	--
Nitrofurantoin	8	+	--	--	--	+	--
Amitriptyline	7	+	+	+	+	+	+
Diazepam	16	+	+	+	+	+	+
Bromazepam	22	+	+	+	+	+	+
Nitrazepam	8	+	+	+	+	+	+
Metoclopramide	24	+	--	--	--	--	--
Loperamide	9	--	+	--	--	--	--
Bisacodyl	5	--	--	--	--	--	+
Trifluperazine	7	+	+	--	+	--	+
Naproxen	8	+	+	+	+	+	+
Piroxicam	8	+	+	+	+	+	+
Diclofenac	29	+	+	+	+	+	+
Tenoxicam	5	+	+	+	+	+	+
Ketoprofen	8	+	+	+	+	+	+
Ibuprofen	22	+	+	+	+	+	+
Pentazocine	12	+	+	+	--	+	--
Codeine	17	+	--	+	--	+	--
Spironolactone >25	15	+	--	+	--	--	--
Cimetidine	3	--	--	--	--	--	+
Fluoxetine	2	--	--	--	--	+	--
Nifedipine [SA]	18	--	--	--	+	+	--
Mineral oil	11	--	--	+	--	--	--
Atorvastatin	48	--	--	+	--	--	--
Prescription quality							
Need additional drug	45	--	--	--	+	--	--
Unnecessary drugs	35	--	--	--	+	--	--
Needs tests	69	--	--	--	+	--	--
Choice of drug	30	--	--	--	+	--	--
Dosage too low	96	--	--	--	+	--	--
Dosage too high	98	--	--	--	+	--	--
Risk of ADR	25	--	--	--	+	--	--
Drug-drug INT	125	--	--	--	+	--	--
PIM [%]		33.4	27.2	32.4	73.2	27.9	22.9

Key: -- = *not applicable*, + = *PIM*, *INT* = *interaction*

The performance of PIM assessment tools vary considerably as they relate to clinically significant drug – drug interactions. Results showed that NORGEP and BENADURS criteria were the most effect with prevalence of 100% and 50.5% respectively. However, Beers criteria and PRISCUS list did not identify any PIM related to drug – drug interactions. Other criteria like STOPP/START and French consensus panel list only produced minimal result of 22.3% and 10.9% PIM prevalence clearly indicating their poor performance is this aspect of PIM evaluation.

Table 3: Prevalence of potential drug – drug interaction using six explicit criteria.

Drug combination [n =220]	N	Beers criteria	STOPP/ START	NORGEP criteria	BEDNURS criteria	PRISCUS List	French consensus Panel list
Lisinopril + Spironolactone	51	--	--	+	+	--	--
Captopril + Spironolactone	51	--	--	+	+	--	--
Valsartan + Spironolactone	4	--	--	+	+	--	--
Amlodipine + Nifedipine	25	--	+	+	--	--	--
Captopril + Naproxen	10	--	--	+	--	--	--
Lisinopril + Piroxicam	10	--	+	+	--	--	+
Piroxicam + Tenoxicam	5	--	+	+	--	--	+
Ibuprofen + Diclofenac	7	--	+	+	--	--	+
Ketoprofen + Meloxicam	2	--	+	+	--	--	+
Naproxen +BDF	5	--	--	+	+	--	--
Metformin + BDF	12	--	--	+	--	--	--
Tenoxicam +Prednisolone	4	--	--	+	--	--	--
Naproxen + Fluoxetine	3	--	--	+	--	--	--
Codeine + Paracetamol	31	--	--	+	--	--	--
PIM [%]		NA	22.3	100	50.5	NA	10.9

Key: -- = *not applicable, + = PIM, BDF = Bendrofluthiazide*

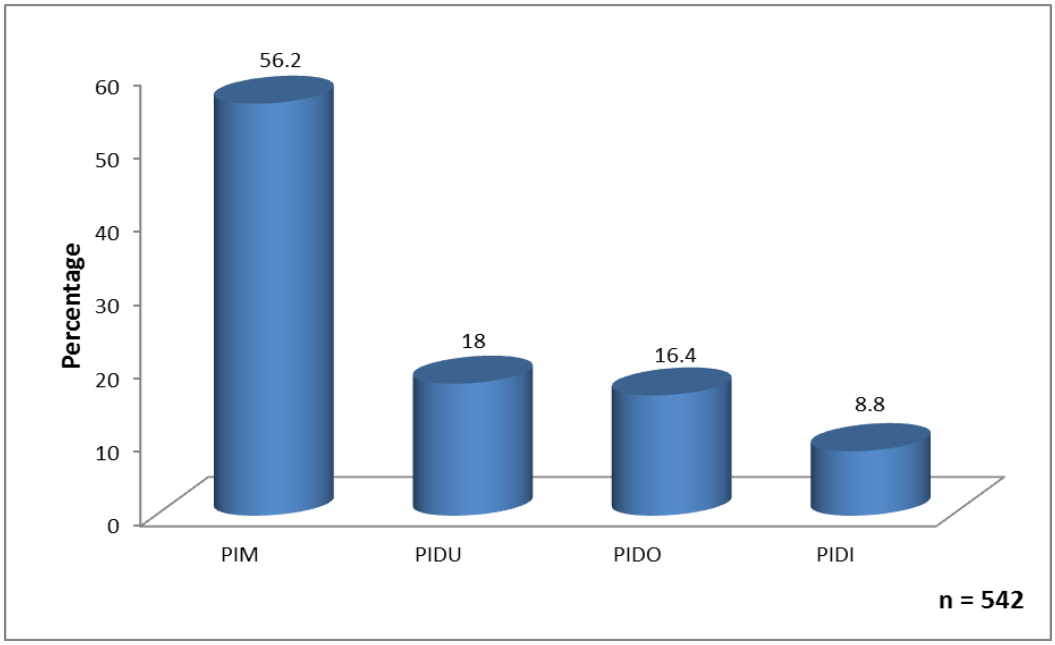
Among the six tools STOPP/START and Beers criteria were comparatively more effective at identifying drug disease interactions. They were used to identify this type of PIM in 100% and 46% of cases respectively. The other tools were ineffective in this type of PIM assessment.

Table 4: Prevalence of potential drug – disease interaction using six explicit criteria.

DRUG	Number	Disease	Beers Criteria	STOPP/ START	NORGEP criteria	BEDNURS criteria	PRISCUS list	French consensus panel list
NSAIDs	[n = 20]							
Naproxen		*CHF*	+	+	--	--	--	--
Piroxicam		PUD	+	+	--	--	--	--
Ketoprofen		*Gout*	+	+	--	--	--	--
Tenoxicam		*CKD*	+	+	--	--	--	--
Diclofenac			+	+	--	--	--	--
Anxiolytics	[n = 8]							
Diazepam		*Dementia*	+	+	--	--	--	--
Bromazepam		*Cognitive decline*	+	+	--	--	--	--
Nitrazepam			+	+	--	--	--	--
Glibenclamide	[5]	*DM2*	--	+	--	--	--	--
Atenolol	[7]	*DM2/ Asthma*	--	+	--	--	--	--
Loperamide	[4]	*Gastroenteritis*	--	+	--	--	--	--
Amlodipine	[32]	*Constipation*	--	+	--	--	--	--
Nifedipine	[6]	*Constipation*	--	+	--	--	--	--
Hyoscine	[16]	*Constipation*	+	+	--	--	--	--
Digoxin 250mcg	[2]	*CKD*	+	+	--	--	+	--
PIM [%]	[100]		46	100			2	

Key: *CKD = Chronic kidney disease, DM2 = Diabetes mellitus type 2, -- = not applicable, + = PIM, PUD = peptic ulcer disease, CHF = chronic heart failure*

The overall PIM prevalence using this criteria is 56.2%, however inappropriate duration and dosage accounted for 18% and 16.4% respectively. The potential for drug interactions was also identified in about 8.8% prescriptions.



Key: ***PIM*** *= potentially inappropriate medication,* ***PIDU*** *= potentially inappropriate duration,* ***PIDO*** *= potentially inappropriate dosage,* ***PIDI*** *=* ***potentially inappropriate drug – drug interaction***

Figure 2: Potentially inappropriate medications using Rancourt criteria.

DISCUSSION

Prevalence of potentially inappropriate medications among the elderly using multiple criteria is high. This result is consistent with several studies, though variable results were obtained with different assessment tools. The overall conclusion points to an endemic problem with prescription medications among this vulnerable population. The most frequently prescribed potentially inappropriate medications [PIM] were NSAIDS, first generation antihistamines and Benzodiazepines in that order of decreasing frequency. This result is comparable to PIM prevalence reported in other previous studies.[58,59] NSAIDs are implicated in other areas such as in duplicate therapy, drug - drug interactions and drug disease interactions. This class of analgesics has been widely used in the treatment and palliative care of pain and muscoskeletal disorders, when used carelessly in the presence of interacting drugs and diseases, they could pose significant risks to the elderly.

The results also showed that overall about half of elderly patients were exposed to at least one or more PIM depending on assessment tool used; this is lower than 70 – 84% earlier reported.[31,60,61,62] A number of other studies had reported lower PIM prevalence[48,63,64,65,66], however PIMs` higher than 80% have been reported in several previous studies.[67,68,69,70] Prevalence of PIMs vary widely and are generally influenced by study settings, assessment tool, characteristics of elderly patients, morbidity pattern, healthcare facility and place of residence.[71]

Another critical factor contributing to variations in PIM prevalence relates to absence of consensus on criteria and evaluation methods.[72] Despite the diversity of factors and the potential impact on prevalence rates, there is consensus that PIM among the elderly population is high and is contributing significantly to their morbidity and mortality.[73] Exposure to more PIMs is often associated with higher risk of adverse drug events, result showed that more than a third of patients had one PIM and another fifteen percent have been prescribed two or more PIMs which is higher than previously reported.[74,75] This has the potential to significantly increase drug misadventures among these elderly patients. The average number of drugs per prescription in this study is comparable to previous studies[70], but lower than 3 – 4 earlier reported.[59,76,77]

Identification and preventing PIM is an essential component of preventing drug misadventures and their consequences on the wellbeing of the elderly.[78,79] The overall PIMs identified showed that NORGEP, BEDNURS and STOPP/START criteria produced the highest prevalence of PIMs suggesting that they may be better suited for the study setting.[80] There has been some debate about suitability of some criteria in specific settings[42,44,72], so in the absence of national criteria most studies in Nigeria have relied on Beers and STOPP/START criteria for assessment of PIMs.[59,70,77,81]

All PIM assessment tools have inherent weaknesses which are again demonstrated in the result of this study. A drug may be acceptable with one tool but contraindicated with another assessment tool. Five tools used in this study identified between 22 – 33% of PIMs when it related to individual drugs; however BEDNURS criteria identified more PIMs because it has other considerations which are not found in the other tools. PIMs related to drug-drug interactions was better

identified with NORGEP and BEDNURS criteria, while in the case of drug disease interactions STOPP/START and Beers criteria performed far better than the other criteria.

The inherent deficiencies of these PIM assessment tools have been widely reported in literature.[42,43,45,47] For instance, Beers criteria, PRISCUS list and French consensus panel list are deficient in identifying drug – drug interactions, while STOPP/START criteria also have challenges with identifying PIM issues relating to appropriateness and indications etc. Other tools like NORGEP and BEDNURS criteria are effective in detecting drug – drug, drug - disease interactions as well as other considerations related to indications, effectiveness and safety.

While research using Rancourt criteria are not widely reported in literature, the tool adopted a different approach that emphasizes appropriateness of not only the medication, but also dosage, duration of treatment and absence of interactions. PIM prevalence using this tool produced comparable results with an earlier study, though errors in dosage and duration of therapy in this study were comparatively higher.[48]

It is important to exercise caution in comparing results from diverse tools because PIM prevalence vary even with versions of the same criteria.[82] The used of explicit criteria to evaluate PIM is important but must be seen from the background that most of them do not deal with how drugs are used and clinical conditions that warrant their use, but rather dwell on the drug itself.[83] It is therefore instructive to recognize that rigid application of any one tool may not be suitable in all settings and may in fact be at variance with drug related needs of specific patients. It is imperative that geriatric specialists are involved in the management of elderly patients using current clinical best practice approach so as minimize exposure to potential harmful medications being prescribed for elderly patients.

CONCLUSION

Prevalence of potentially inappropriate medications among the elderly is high irrespective of assessment tool employed. It is important to improve drug prescription habits meant for the elderly so as to reduce the risk of adverse drug events.

Conflict of interest: The authors declare no conflict of interest.

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