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## Drug Therapy Problems in Patients with Type-2 Diabetes in a Tertiary Hospital in Nigeria

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### **Abstract:**

**Background:** Patients with Type-2 diabetes mellitus (T2DM) are known to be at risk of drug therapy problems since they often receive multiple medications due to co-morbidities associated with the condition. This study assessed the prevalence of drug therapy problems and related factors in a population of diabetic patients in a tertiary hospital.

**Methods:** A retrospective analysis of randomly selected medical records of Type 2 diabetic patients was conducted from February to September, 2013. Data was collected and analyzed for demographics, clinical conditions (co-morbidity), types of medications used and medication complications.

**Results:** 399 patients with a total of 792 drug therapy problems were identified, averaging  $2.1(\pm 1.4)$  problems per patient. There were more males (52.1%) than females (47.9%) diabetics. Mean age of the patients was  $65(\pm 12.4)$  years, ranging from 35 to 91 years. 49(12.4%) of the patients experienced at least one episode of hypoglycemia. Non-adherence was the most common DTP at 26.7% while polypharmacy was identified as a major factor that contributed to DTP among the patients.

**Conclusion:** Findings suggest significant incidence of DTPs in the health facility indicating the need for comprehensive medication management approach which requires the use of pharmacists to play more active roles in managing patients with diabetes.

**Key words:** Drugs therapy problems, Type 2 diabetes, polypharmacy, comorbidity, Nigeria

### **1. Introduction**

Diabetes is a leading cause of illness and death in our society, consuming a significant amount of resources through treatment and prevention. Diabetes Mellitus, commonly referred to as diabetes is a condition in which the pancreas no longer produces enough insulin or cells stop responding to the insulin that is produced, so that glucose in the blood can no longer be absorbed into the system (Rogers and Cate 2007). Symptoms include frequent urination, lethargy, excessive thirst, and hunger. Type-2 Diabetes Mellitus (T2DM) is the most common form of diabetes sometimes called age-onset or adult-onset diabetes. It is a milder form of diabetes because of its slow onset (sometimes developing over the years) and because it usually can be controlled with diet and oral medications. The consequences of uncontrolled and untreated T2DM, however, are just as serious as those of Type I. The causes of Diabetes Mellitus are unclear. However, there seem to be hereditary (genetic factors) and environmental factors involved (Rogera and Cate 2007). T2DM is a chronic medical condition that requires regular monitoring and treatment throughout patient's lifetime. The treatment includes changes in diet, oral medications, and in some cases, daily injections of insulin.

Different approaches are adopted in the management of T2DM. Direct treatment focuses on treatment with oral antidiabetics generally referred to as hypoglycemic agents. Patients with T2DM receive a wide range of pharmacotherapeutic agents due to the presence of other medical/co-existing conditions (co-morbidity) and are therefore often at high risk of experiencing drug therapy problems (DTPs). A DTP occurs as an undesirable event or risk experienced by a patient, which involves or is suspected to relate to drug therapy (Strand et al., 1990). The event could prevent or delay the achievement of desired therapeutic goals in patients. While an actual DTP occurs when an event has already occurred in a patient, a potential DTP is an event that may likely develop if appropriate interventions are not promptly provided (Revert et al., 2004). Examples of DTPs usually encountered in practice include, the use of unnecessary or wrong drugs, adverse drug reactions, dosage too high, dosage too low, non complication and need for additional therapy (Strand et al., 1998).

Many factors have been identified to contribute to the development of DTPs in T2DM patients. These include co-morbidity, polypharmacy, age, medical conditions, and renal impairment. Hypertension is a common co-morbidity in T2DM, often prevalent in up to 75% of the diabetic population (Huri and Wee 2013) and may be present at the time of T2DM diagnosis or even before onset of disability, enhancing the risk of cardiovascular disease in T2DM patients (ADA, 2012). Given that a number of drugs are given to diabetic hypertensives to achieve optimal reduction of BP (Munga 2010), this increases the number of medications given to the diabetics, further exposing them to the risk of DTPs

Polypharmacy involves concomitant medications of up to five or more drugs, inherent in hypertensive diabetics. Increasing age of about 65 years and above is a factor associated with multiple medical conditions, multiple drug therapy and age-related changes in drugs pharmacokinetics and pharmacodynamics (Munga 2010). Multiple medical conditions and renal impairments are known to contribute significantly to DTPs (Blix et al., 2004). Studies have shown that patients with end stage renal disease (ESRD) are also among those at high risk for DTPs (Grabe *et al.*, 1997; Manley *et al.*, 2003b).

Generally DTPs pose significant challenges to health care providers and patients alike, contributing to morbidity or mortality, prolonged hospitalization, and increased health care expenditure if left unresolved (Ernst and Grizzle 2001). However, DTPs are preventable in most cases (Leendertse et al., 2008).

In Nigeria limited studies exist that have documented the incidence of DTPs among T2DM patients. In one such study, Odili et al. 2011 identified a high incidence of DTPs in Type 2 diabetic patients admitted in a secondary healthcare facility in Benin City, south-south Nigeria. This study was aimed at identifying the incidence of drug related problems among T2DM patients treated at a tertiary hospital, south-east Nigeria, as well as the factors influencing these problems, to document information for improving the quality of life of diabetic patients in Nigeria.

## 2. Study Design and Methods

### 2.1. Study Design and Setting

A retrospective study involving the review of the records of patients admitted at a diabetes ward of a tertiary health facility, Nnamdi Azikiwe University Teaching Hospital, (NAUTH) Nnewi, was conducted covering a period of six months, (between February and September, 2013).

### 2.2. Study Site and Population

NAUTH is a tertiary health institution located at the commercial city of Nnewi, Anambra state, south-east Nigeria. The state has a population of about 4.1million people who are mainly involved in farming, trade and commerce. The hospital has a 500-bed capacity, providing highly specialized clinical services, research and training. A total of 399 prescription records and folders of Type 2 diabetic patients from diabetic ward of the hospital were randomly selected for the study. The sample size was informed by the method adopted by the Centers for Disease Control and Prevention, Atlanta GA, which provided a minimum sample size of 195 patients. The study population consisted of T2DM patients who were admitted at the hospital between the months of February and September 2013. Inclusion criteria were prescriptions of patients diagnosed with T2DM, prescription of patients who received at least one anti-diabetic drug (Oral anti-diabetic drug or insulin) in the ward and adult patients aged 18 years old and above. Exclusion criteria was prescriptions with incomplete data

### 2.3. Data Collection

Data were collected from prescriptions, patients' folders and case notes. Prescribers' assessment of patients was noted as the indication for drug therapy. Demographic characteristics such as age and gender were recorded. Clinical characteristics such as duration of T2DM, presence of diabetic complications, presence of comorbidities, laboratory results and concurrent medications were also collected.

### 2.4. Evaluation of DTPs

Analysis of data for DTPs was based on the process of classification, identification and assessment of DTP. We first categorised DTPs using the established system developed by The Pharmaceutical Care Network Europe (PCNE) classification of drugs related problems (DRPs) version 5.01 (PCNE, 2006), also used by many studies in recent publications (Huri and Wee 2013; Chan et al., 2011; Eichenberger et al., 2010; van Roozendaal et al., 2009). In our study we used six domains to classify and identify the observed DTPs and their possible causes from the patients' medical records, based on established standard guidelines. Appropriateness of drug

indications, drug usage and dosage, possible drug interactions, adverse drug reactions and contraindications were assessed using references (BNF, 2010; Lucy et al., 2012)

Modified Beers criteria, which is a consensus-based drug list that includes the list of drugs that should be avoided or used with cautious care in the elderly (Huri and Wee 2013) was used as a reference to assess and identify the potential drugs that were inappropriately used in the patients aged 65 years and above. The drugs were divided into low and high risks. In our study only inappropriate prescriptions of Beers criteria for high severity drugs were identified as DTPs, because they might pose significant adverse events when used in the elderly.

### 2.5. Statistical Analysis

Our study used the Statistical package for Social Science (SPSS) version 16 (SPSS Inc., Chicago, IL, USA) to analyze all collected and extracted data. Categorical data were expressed as percentages and continuous data were expressed as mean and standard deviation. Statistical significance was defined as p-value < 0.05.

### 2.6. Ethical Issues

Approval from the hospitals research and ethical committee was obtained before the commencement of the study. Utmost confidentiality of information was also maintained by excluding patients' name and any other information that may be linked to them.

## 3. Results

Table 1 shows the demographic and clinical characteristics of the patient population studied. The study analysed a total of 399 patient records, consisting of 208 (52.1%) males and 191 (47.9%) females (Table 1). Average age of the patients was 65 ( $\pm$  12.4 ) years, varying from 35 to 91 years, but majority of the patients (30.3%) fell within 71 – 80 years. Mean duration of treatment was 9.8 ( $\pm$ 5.7) years per patient. Table 1 shows that in majority of the diabetic patients (66.7%), the hemoglobin A1c, (used as a primary test for diabetes management) was above 6.5 while about 51% of the patients with hypertension have their blood pressure above target level of 120/80 mmHg. A total number of 792 DTPs across the six categories were identified in 94% of the patients, averaging 2.1 ( $\pm$ 1.4) problems per patient.

Characteristics	Number of patients	Percentage (%)
<b>Sex</b>		
Male	208	52.1
Female	191	47.9
<b>Age (Years)</b>		
<40	12	3.0
40-50	58	14.5
51-60	88	22.1
61-70	104	26.1
71-80	121	30.3
81-90	16	4.0
<b>Duration of T2DM (Years)</b>		
5	114	28.6
10	189	47.4
15	53	13.3

16-20	32	8.0
21-25	5	1.3
26-30	6	1.5
<b>A1c</b>		
Achieved target (<6.5)	133	33.3
Not achieved target ( $\geq 6.5$ )	266	66.7
<b>BP(mmHg)</b>		
HBP $\geq 140/90$	203	50.9
HBP $\leq 120/80$	196	49.1

Table 1: Demographics and clinical parameters of study patients (N = 399)

Table 2 presents the list and proportion of DTPs associated with the T2DM patients identified in the hospital during the period. Non-compliance was the most common DTP occurring within the study patients at 26.1%, it was followed by the use of unnecessary/ineffective drugs and need for additional drugs respectively. Too low dosage problems were the least occurring DTP at 8% frequency

Categories of DTP	No of problems (%)
Adverse drug reaction (ADR)	49 (12.3)
Need for additional drug therapy	81 (20.3)
Ineffective/unnecessary drug	91 (22.8)
Dosage too high	42 (10.5)
Dosage too low	32 (8.0)
Non-compliance	104 (26.1)

Table 2: Drug therapy problems associated with the T2DM patient population

The class of drugs used in the T2DM patients who were associated with DTPs is presented in Table 3 below. Endocrine drugs such as oral hypoglycaemic agents were the most commonly used drugs associated with DTPs, identified in 28.7% of the study population. They were followed by analgesics (14.4%) and anti-infective drugs (14.2%), respectively.

Therapeutic group	Number (%)
CNS drugs	78 (3.8)
Anti-infective	292 (14.2)
Endocrine drugs	591(28.7)
Analgesics	297 (14.4)
GIT drugs	193 (9.4)
Others steroids	89 (4.3)

Vitamins	211(10.3)
Anti-malarial	79 (3.8)
Insulin	198(9.6)
Others	30 (1.5)

*Table 3: Therapeutic group associated with DTP (N=2058)*

Table 4, which lists the common co-existing conditions associated with T2DM, shows that hypertension was the highest co-morbidity, existing in 53% of the patients.

<b>Comorbidity</b>	<b>Number of diabetic patients (%)</b>
Hypertension	212 (53.1)
Hypertension with viral hepatitis	41 (10.3)
Cellulitis	8 (2.0)
Hypertension with cardiovascular disease	31 (7.8)
Only diabetics	107 (26.8)

*Table 4: Comorbidity associated with the T2DM patients*

A total of 1159 antidiabetic drugs were used by the study population within the period. In Table 5 is presented the list and frequency of use of antidiabetic drugs. Metformin, a biguanide was the most commonly used antidiabetics in 27.6% of the prescriptions. It was followed by Glibenclamide used in 22.5% of the time. A combination of metformin and glibenclamide was prescribed for 6.6% of the patients. Insulin injection was prescribed for 17.1% of the patients

<b>Antidiabetic Used</b>	<b>Number (%)</b>
Metformin	320 (27.6)
Glibenclamide	261 (22.5)
Alphabetic	74 (6.4)
Glimepiride	198 (17.1)
Glipizide	0 (0.0)
Pioglitazone	32 (2.8)
Insulin	198 (17.1)

Glibenclamide+Metformin	76 (6.6)
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*Table 5: Types of antidiabetics used*

Using the Modified Beers criteria to identify inappropriate use of medications among the elderly patients, the study showed that 16 medications were found to have been used inappropriately (Table 6). While 14 of these medications were identified as high severity occurrence, two medications occurred under the potentially low severity cases. Promethazine was the most used high severity inappropriate medication occurring in 27.8% of the cases while cimetidine was prescribed in 75% of the cases under potentially low severity occurrence

<b>High severity potentially inappropriate medications</b>	<b>Number of prescriptions (%)</b>
Promethazine	31(24.8)
Diazepam	12(9,6)
Amitriptyline	8(6,4)
Bromazepam	8(6,4)
Nitrazepam	6(4,8)
Phenobarbitone	9(7,2)
Lorazepam	1(0,8)
Methyldopa	16(1,3)
Naproxen	2(1,6)
Sodium valproate	7(5,6)
Pregabalin	3(2,4)
Carbamazepine	7((5,6)
Bisacodyl	2(1,6)
Pentazosine	13(10,4)
<b>Low severity potentially in appropriate medications</b>	
Dypiridamole	2(25)
Cimentidine	6(75)

*Table 6; Occurrence of potentially inappropriate medications*

#### 4. Discussion

Results suggest that diabetes is more prevalent among the age group of 71 – 80 years in our study where the ages averaged of 65 years. This is quite different from the results of similar studies in other developing countries (Ebenezer et al., 2003; Huri and Wee 2013; Letchuman et al., 2010; Odili et al., 2011) which reveal a prevalence of diabetes between 45 and 64 years. The difference might be explained by the fact that the sample may not be representative of the whole population. The result would also suggest that more older diabetics than the younger ones were admitted at the hospital during the period (Huri and Wee 2013). The findings that male

diabetics were more than females is consistent with some studies (Odili et al., 2011) but inconsistent with others (Omole et al., 2012; Ebenezer et al., 2003).

Pattern of prescription from the study showed an average number of 5.8 drugs per prescription with some prescriptions containing up to 9 drugs per patient, giving an indication of polypharmacy, which increases the risk of DTP such as adverse drug reaction. This is consistent with the findings of many studies (Blix et al., 2004; Leendertse et al., 2008; Viktil et al., 2007). Polypharmacy is strongly associated with DTPs with evidence that a one unit increase in the number of drugs can lead to an increase of 8.6% in the number of DTPs (Viktil et al., 2007). Increase in the number of drugs used can lead to increased risk of potential drug interactions (Aparasu et al., 2007; Delafuente, 2003), poor glycemic control and poor therapeutic outcomes. Since polypharmacy is an inherent problem in T2DM due to associated co-morbidities, there is need for routine monitoring and checking of clinically important and significant drug interactions. This calls for the important role of the pharmacists in identifying such cases and reporting and correcting accordingly. The need for more careful diagnoses and rational prescription, dispensing and use of drugs is emphasized.

Results show that hypertension was the most common co-existing condition in more than half of the diabetic patients. This is consistent with several studies of T2DM (Omole et al., 2012; Osiliet al., 2011). Analysis of the antihypertensive medications used suggests that the most frequently used class of drugs were Angiotensin enzyme inhibitors (ACEIs), calcium channel blockers (CCBs) and diuretics. In diabetic patients with hypertension, a target reduction of blood pressure (BP) of  $\leq 130/80$  mm Hg is often recommended, as a guideline to minimize the risk of complications (ADA, 2012). However, achieving this can be challenging as majority of patients require one or more antihypertensives for optimal control of BP (Munga 2010). This may possibly explain the fact that in this study the blood pressures of almost more than half of the patient population remained above the recommended target (Table 1), which is also consistent with similar studies in Nigeria and other developing countries where the blood pressures of the majority of diabetic hypertensives have been shown to be poorly controlled (Omole et al., 2012)

Among this group of hypertensive diabetics were 31 cases of those with cardiovascular diseases who were observed to have had more DTPs than those without cardiovascular conditions. This is not surprising considering that their condition required the use of a wide range of cardiovascular drugs such as anticoagulants, anti-platelet drugs, and lipid lowering drugs, in addition to antihypertensives and antidiabetics, increasing the risk of drug interactions and DTPs

The fact that elderly patients with T2DM have been shown to particularly be at risk of developing diabetic complications such as hypoglycaemia, ocular complications and diabetic foot ulcers (Fletcher and Dolben 1996; Huminar et al., 1989; Seltzer 1989), was demonstrated in this study. Oral hypoglycaemic agents with a long half-life (such as glibenclamide or chlorpropamide) can cause potentially dangerous hypoglycaemia (Seltzer 1989; Sugarman 1991). In our study about 12.4% of the patients experienced at least one episode of hypoglycaemia, where glibenclamide was the second most prescribed antidiabetics in the hospital. Diabetic retinopathy and foot ulcers were also identified as some of the complications in the study resulting from inappropriate use of drugs. The fact that these complications were common among the older patients than younger cases indicates the impact of age on DTPs. It suggests the need for more careful selection of oral antidiabetics in the elderly, replacing the long-acting agents with short-acting ones such as gliclazide (Fletcher and Dolby 1996). The patients should be more closely monitored to prevent occurrence.

The study identified more than about 792 drug related problems across the six categories of DTPs, giving an average of 2.1 problems per patient. Non-compliance, unnecessary drugs and the need for more drugs were the most frequent categories of DTPs identified. Most of the patients lacked understanding of the disease state and the management, which contribute to non-adherence (Ali et al., 2009), being ignorant of the consequences. The study by Ali et al is particularly true for the elderly who tend to have reduced memory, poor health practices, poor adherence to medications and dietary control. Counseling and diabetic education may be important to increase the awareness and knowledge of this patient population. Studies, particularly in Nigeria have documented non-adherence as a major concern in the treatment of patients with T2DM (Omole et al., 2012; Odili et al., 2011). There is therefore the need for effective counseling and diabetic education of the patients to enhance their awareness and knowledge of the condition for improved adherence.

Use of unnecessary drugs was the second most common DTP recorded. Some drugs were prescribed without any clear indication and as such, questionable since they have been found to be associated with increased pill burden, polypharmacy and non-adherence. Prescribing of two different analgesics simultaneously to treat the same condition was also identified.

The need for additional drug therapy was the third most frequent DTP in the hospital. Some of the patients were not receiving antiplatelet therapy even when they were at high risk of cardiovascular complications. The study also showed that some patients did not receive antihypertensive therapy even when there was a clear indication of hypertension. This may partly explain the high number of the patients whose BPs were higher than normal levels.

ADRs occurred in a significant number of the diabetic patients (12%) also treated for hypertension. This was not surprising as the three most commonly used antihypertensive agents, ACEIs, CCBs and diuretics are known to cause ADRs (Huri and Wee 2013). However the CCBs are known to cause higher incidence of ADRs than the diuretics (Goncalves et al., 2007). The "triple whammy effect" (use of ACEIs, thiazide diuretics and NSAIDs) was observed in a few cases and this poses a potential for DTP that can cause a two fold increase in the risk of hospitalization in diabetic patients with hypertension (Heerdink et al., 1998). However majority of the ADRs identified in the study were caused by antidiabetics and most of these were hypoglycaemia. Potential adverse reactions should be taken into consideration, especially in the elderly who might suffer significant deleterious side effects (Huri and Wee 2013)

Based on the Beers criteria, our study showed a significant number of potentially inappropriate medications which may pose high and low risks of DTPs in the elderly. The use of promethazine occurred most as high severity, followed by pentazocine and diazepam respectively. Under the criteria high severity were identified as DTPs because of the high risk of adverse effects associated with them

when used in the elderly (Fick et al., 2003; American Geriatrics Society, 2012) especially in type 2 diabetes patients. This suggests the need to use these drugs with cautious care or avoided completely.

Our findings and discussions above suggest that age, polypharmacy, cardiovascular disease, renal impairment, and duration of state are all associated with DTPs at varying degrees. While many studies have reported direct association between age and DTPs (Chen et al., 2007; Viktil et al., 2007; Huri and Wee 2013) others did not quite agree (Koh et al., 2005; Blix et al., 2004). In our study most of the reported complications occurred in the older patients. The study also identified diabetic nephropathy as one of the commonest complications. Observation of this group shows that drug dosages were higher than required. Studies have shown that diabetic patients on hemodialysis were more likely to experience DTPs (Huri and Wee 2013; Leendertse et al., 2008). The study by Leendertse et al. found that impaired renal function was a risk factor

for potentially preventable DTPs. This suggests that adjustment and close monitoring of renal function are important to prevent complications. In our study, a significant number of diabetic hypertensives who have cardiovascular complications experienced DTPs. The incidence of DTPs in this group can be explained by the use of many cardiovascular drugs which included antiplatelet drugs, anticoagulants, and lipid lowering drugs in the patients with hypertension.

Generally our study findings suggest that DTPs are caused by a variety of factors which can be said to be drug related or patient related. Drug related causes are either based on the problem of selection of dosage problems. Patient related causes arise from the process of drug use, lack of information and patient physiological factors (PCNE, 2006). Our study results suggest that drug related causes were the most frequently identified causes based on the categories of DTPs.

The causes and prevalence of DTPs among T2DM patients which is significant, emphasizes the need for more efforts at improving the management of T2DM in the hospital. It calls for more effective identification, management and prevention of the incidence to improve the quality of life of the patients who have to live with the condition/s throughout their lifetime in view of the chronic nature of the disease. Current approach focuses on medication management involving treatment of T2DM patients with the provision of comprehensive medication therapy management (Cipolle et al., 2013). This is a patient centered service involving comprehensive evaluation of patients' medications and their impact on patients' multiple conditions. This strategy, known as Comprehensive Medication Management Services focuses on identification, resolving and preventing DTPs (Cipolle et al., 2013). Pharmacists have been known to play important roles in resolving DTPs through direct communication with the patients, in 87% of the cases (Grabe et al., 1998; Cipolle et al., 2011). The comprehensive medication management approach allows the pharmacist to play more active roles in helping to manage the patient through a standard patient care process focused on identifying, resolving and preventing drug therapy problems. Each patient's prescription is assessed to determine if any of the medications are inappropriate, ineffective, unsafe or inconvenient for the patient to take as required. Whenever drug therapy problems are identified, they are resolved by changing the drugs, doses, or by educating the patient on how to effectively maximize the use of the medication (Cipolle et al., 2013)

## 5. Limitations of the Study

Our study was retrospective, relying only on information available in the hospital records. Direct information from patients may have been useful to add to the hospital records. The study did not collect information on duration of stay to further explain the impact on DTPs. Our assessment may not have been comprehensive enough to generate adequate information as a baseline data for further studies and comparative purposes. While our study findings were similar in many respects to similar studies, discrepancies exist that would be attributed to the differences in the methods of study, study settings and study populations. Of particular mention are the differences in classification of DTPs, which vary between studies, leading to differences in identification of type and number of drug related problems hence, discrepancy in many study results. Differences also exist in the type of references used.

## 6. Conclusion

There is significant incidence of drugs related problems in the management of T2DM in the teaching hospital. Most of these problems which occur mostly in the elderly patients result from co-morbidity, polypharmacy, and inappropriate use of drugs associated with T2DM. Factors such as age, renal impairment, cardiovascular disease are mostly associated with DTPs. Hypertension is the most common co-morbidity in T2DM occurring in over half of the patients and the control of blood pressure among this group is often not optimal. Diabetic patients with hypertension and risk factors who are prescribed commonly implicated drugs require special attention. DTPs were also common among the diabetic patients with renal impairment due to the presence of other medical conditions, as most of them were receiving multiple medications which require dosage adjustment and routine monitoring. Early identification and prevention of DTPs in T2DM and rational use of drugs are necessary to prevent complications and unnecessary hospitalization, high cost of treatment and deaths among diabetic patients. Pharmacists play important roles in identifying and resolving DTPs through direct communications with the patients, as well as other healthcare providers. Current strategy applies the Comprehensive Medication Management Services which focuses on identification, resolving and preventing DTPs through the pharmacists. The approach requires that all of the medications be evaluated for appropriateness, effectiveness, safety and compliance.

## 7. References

1. Ali SM, Jusoff K (2009): Barriers to optimal control of type 2 diabetes in Malaysian Malay patients. *Global Journal of Health Science*, 1(2):P106.
2. American Diabetes Association: Standards of medical care in diabetes- 2012. *Diabetes Care* 2012, 35(Suppl.1):S11-S63.



3. American Geriatrics Society (2012): Updated beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatric Society*, 60:616–631.
4. Aparasu R, Baer R, Aparasu A (2007): Clinically important potential drug-drug interactions in outpatient settings. *Res Social Adm Pharm*, 3(4):426–437.
5. Blix HS, Viktil KK, Reikvam A, Moger TA, Hjemaas BJ, Pretsch P, et al: The majority of hospitalised patients have drug-related problems: results from a prospective study in general hospitals. *Eur J Clin Pharmacol* 2004, 60(9):651–658
6. British National Formulary Joint Formulary Committee: British national formulary. 60th edition. London: British Medical Association and Royal Pharmaceutical Society of Great Britain; 2010.
7. Chan DC, Chen JH, Kuo HK, We CJ, Lu IS, Chiu LS, et al: Drug-related problems (DRPs) identified from geriatric medication safety review clinics. *Arch Gerontol Geriatr* 2011, 54:168–174.
8. Cipolle RJ, Strand LM, Frakes MJ. Co-morbidities and Drug Therapy Problems in Patients with Diabetes. Medication Management Systems, Inc. 2013.
9. Delafuente JC (2003): Understanding and preventing drug interactions in elderly patients. *Crit Rev Oncol Hematol*, 48(2):133–143.
10. Ebenezer AN, Osaretin JO, Anele EI, Aaron O, Seye B (2003). Type 2 diabetes in adult Nigerians: a study of its prevalence and risk factors in Port Harcourt, Nigeria. *Diabetes Res Clin Pract*; 62:177-185.
11. Eichenberger PM, Lampert ML, Kahmann IV, van Mil JWF, Hershberger KE: Classification of drug-related problems with new prescriptions using a modified PCNE classification system. *Pharm World Sci* 2010, 32(3):362–372.
12. Ernst FR, Grizzle AJ: Drug-related morbidity and mortality: updating the cost-of-illness model. *J Am Pharm Assoc* 2001, 41(2):192–199.
13. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH, et al (2003): Updating the beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Med*, 163(22):2716–2724.
14. Fletcher A, Dolben J. A Hospital Survey of the Care of Elderly. Patients with Diabetes Mellitus. Age and ageing, 1996;25:349-352
15. Zaman Huri and Fun Wee: Drug related problems in type 2 diabetes patients with hypertension: a cross-sectional retrospective study. *BMC Endocrine Disorders* 2013 13:2.
16. Helper CD, Strand LM (1990). Opportunities and responsibilities in pharmaceutical care. *Am J Hosp Pharm*.; 47:533-43. <http://www.biomedcentral.com/1472-6823/13/2>
17. Huminer D, Dux S, Rosenfeld JB, Pitlik SD. Inadvertent sulfonylurea-induced hypoglycemia: a dangerous, but preventable condition. *Arch Intern Med* 1989; 149:1890-2.
18. Koh Y, Kutty FBM, Li SC: Drug-related problems in hospitalized patients on polypharmacy: the influence of age and gender. *Ther Clin Risk Manag* 2005, 1(1):39–48.
19. Lacy CF, Armstrong LL, Goldman MP, Lance LL: Drug information handbook. 20th edition. Lexi-Comp Inc: Hudson, Ohio; 2011.
20. Leendertse AJ, Egberts ACG, Stoker LJ, van den Bemt PMLA: Frequency of and risk factors for preventable medication-related hospital admissions in the Netherlands. *Arch Intern Med* 2008, 168(17):1890–1896
21. Letchuman G, Nazaimoon WMW, Mohamad WBW, Chandra L, Tee G, Marshall SM, Flyvbjerg A (2006). Prevention and early detection of vascular complications of diabetes. *BMJ*: 475-80.
22. Letchuman G, Nazaimoon WMW, Mohamad WBW, Chandran L, Tee G, Jamaiyah H, et al: Prevalence of diabetes in the Malaysian national health morbidity survey III 2006. *Medical Journal of Malaysia* 2010, 65(3):173–179
23. Munger MA: Polypharmacy and combination therapy in the management of hypertension in elderly patients with Co-morbid diabetes mellitus. *Drug Aging* 2010, 27(11):871–883.
24. Omole MK, Ahwinahwi US, Adeleye J. Knowledge of the disease and adherence to drug therapy among patients with Type 2 diabetes and hypertension. *Glo J Med Res* (2012), 12:2(1): Accessed online @
25. PCNE%20classification%20V5.01.pdf.
26. Pharmaceutical Care Network Europe Foundation: PCNE classification for drug-related problems V5.01. 2006. <http://www.pcne.org/sig/drpf/documents/>
27. Seltzer HS. Drug-induced hypoglycemia: a review of 1418 cases. *Endocrinol Metabol Clin North Am* 1989;18:163-83
28. Strand LM, Cipolle RJ, Morley PC, Frakes MJ (2004). The impact of pharmaceutical care practice on the practitioner and the patient in the ambulatory practice setting: Twenty-five years of experience. *Curr Pharm Des.*; 10:3987-4001.
29. Sugarman R. Hypoglycemia associated hospitalizations in a population with a high prevalence of non-insulin dependent diabetes mellitus. *Diabetes Res Clin Pract* 1991; 14:139-47.
30. Van Roozendaal BW, Krass I: Development of an evidence-based checklist for the detection of drug related problems in type 2 diabetes. *Pharm World Sci* 2009, 31(5):580–595.
31. Viktil KK, Blix HS, Moger TA, Reikvam A: Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. *Br J Clin Pharmacol* 2007, 63(2):187–195