Comparative drug therapy problems and pharmacists' intervention in selected health facilities in Ogun State Nigeria.

Soremekun Rebecca[1], Miftah Luqman[2] and Oreagba Ibrahim[3]
[1]Department of Clinical Pharmacy and Biopharmacy, University of Lagos
[2] West African Postgraduate College of Pharmacy
[3] Department of Pharmacology, Therapeutics and Toxicology University of Lagos

Corresponding Author: Rebecca Soremekun
Email: rsoremekun@unilag.edu.ng Phone: 08033186457

ABSTRACT

Background - Regular medication reviews will reduce the occurrence of Drug Therapy Problems (DTPs). This study set out to identify, document DTPs and evaluate the impact of pharmacists´ interventions in selected health facilities.

Methods - The study was carried out simultaneously at two tertiary and two secondary hospitals in Ogun States. Pharmacists were trained to document all identified DTPs in prescriptions and impacts of pharmacists' interventions for six months using the documentation form, PCNE V5.01. Data was analyzed and presented as frequencies with test of significance of main parameters.

Results – One hundred and four (104) DTPs were reported in all the health facilities but with no significant difference in occurrence at the two hospital levels. Commonly occurring DTPs were drug choice problems (35.6%), dosing problems (33.9%), adverse drug reaction (22.8%), drug use problems (4.23%) and drug interactions (1.69%). Most proposed interventions (77.0%) were approved by prescribers with (77.2%) resolution of DTPs in tertiary hospitals.

Conclusion- There was no significant difference in occurrence of DTPs in the hospitals but there was higher incidence of non-allergic ADR, contraindication, duration of drug use and duplication of drugs at the secondary level. Acceptance rate of proposed interventions by physicians was high (77.2%) confirming that pharmacists' intervention in rational pharmacotherapy is valuable.

Key Words: drug therapy problems; tertiary hospital; secondary hospital

Comparatifs des problèmes de traitement médicamenteux et l'intervention des pharmaciens dans les établissements de santé sélectionnés dans l'Etat d'Ogun au Nigeria.

Auteur correspondant: Rebecca Soremekun
Email: rsoremekun@unilag.edu.ng Téléphone:08033186457

Contexte - Des examens de médicaments permettra de réduire la survenue de problèmes pharmacothérapie (DTP). Cette étude visait à identifier, documenter et évaluer DTP l'impact des interventions de pharmacists' dans les établissements de santé sélectionnés.

Méthodes - L'étude a été réalisée simultanément à deux tertiaire et deux hôpitaux secondaires dans Ogun. Les pharmaciens ont été formés pour documenter tous les DTP identifiés dans les prescriptions et les impacts des interventions des pharmaciens pendant six mois en utilisant le formulaire de documentation, PCNE V5.01. Les données ont été analysées et présentées sous forme de fréquences avec test de signification des paramètres principaux.

Résultats - Cent quatre (104) DTP ont été signalés dans tous les établissements de santé, mais sans différence significative dans la survenue aux deux niveaux de l'hôpital. Communément DTP survenus étaient des problèmes de drogue de choix (35,6%), les problèmes de dosage (33,9%), les effets indésirables des médicaments (22,8%), les problèmes de consommation de drogues (4,23%) et les interactions médicamenteuses (1,69%). La plupart des interventions proposées (77,0%) ont été approuvés par les prescripteurs avec (77,2%) la résolution du DTP dans les hôpitaux tertiaires.

Conclusion- Il n'y avait pas de différence significative dans la survenue de la DTP dans les hôpitaux, mais il y avait une incidence plus élevée de non-allergique ADR, contre-indication, la durée de l'usage de drogues et la duplication des médicaments au niveau secondaire. Taux d'acceptation des interventions proposées par les médecins était élevé (77,2%) confirmant que l'intervention de pharmaciens en pharmacothérapie rationnelle est précieux.

Mots clés: problèmes de traitement médicamenteux; hôpital tertiaire; hôpital secondaire

INTRODUCTION

The potential for sub-optimal outcomes of therapy may be assumed with drug administration, it is therefore important to be watchful for potential and actual drug therapy problems. DTPs are known to prevent patients from realizing the full benefits of their drug therapy.[1] They can originate from prescription, dispensing, administration of medicines or from gaps in the continuity of care and the commonality of occurrence has been reported in primary and secondary hospital settings.[2, 3] Potential and actual DTPs can be identified and problems prevented by pharmacists through medication profile reviews and monitoring of therapeutic plans while resolutions can be effected through interventions such as patient counseling and recommendations to prescribers. In hospital and community pharmacy settings, the reduction of the occurrence and or resolution of DTPs through pharmacists´ interventions have been well documented and have proven to be valuable contributions to positive patient care outcomes.[4,5,6,7] Multi-professional collaborations (including pharmacists), have resulted in beneficial therapeutic effects. These studies have reported positive effects on patient safety through reduction in ADRs, reduction in drug costs and healthcare utilization as well as appropriateness of prescribing.[8, 9, 10] The mode of intervention is also an important factor in possible outcome When the pharmacists' recommendations are discussed face-to-face rather than presented in writing and when the inter-professional team is well established and builds on mutual trust, then the acceptance rate is increased.[11, 12]

Hospital wide review of drug therapy problems and pharmacists' intervention have not been reported in many health care facilities in Nigeria. It is against this background that this study was carried out to contribute to data on and improve knowledge and awareness of pharmacists on the identification of DTPs. This study was specifically aimed at comparing the rate of occurrence of DTPs and resolution of same by pharmacists in selected tertiary and secondary health facilities in Ogun state, Nigeria.

METHODS

Study Design - The study comprised of an educational intervention and a prospective cross – sectional survey in selected health facilities. Prior to data collection, pharmacists in the health facilities were trained on the concept of DTPs, documentation and intervention processes using the PCNE form V5.01 with the aid of a case study.[13] Pre and Post-test questionnaires were administered during the training. The pharmacists then reviewed all out-patient and in-patient prescriptions dispensed within the study period (June-Dec 2013) to identify and document DTPs and interventions.

Study Setting -Ogun state has three tertiary hospitals, ten secondary health facilities and five primary health centers. The study was carried out in two purposively selected tertiary hospitals; Federal Medical Center Abeokuta (FMCA) and Olabisi Onabanjo University Teaching Hospital Shagamu (OOUTHS) and two secondary hospitals; State Hospital, Abeokuta (SHA) and State Hospital Ijebu-Ode (SHIO) all in Ogun state, South-West of Nigeria.

Sampling techniques and sample size determination – A purposive sampling technique was utilized to select the two tertiary and two secondary health facilities that served as the study sites from among the health facilities in Ogun State.

The average number of prescriptions per day in the hospitals' out-patient and in-patient units were FMCA - 360, OOUTHS - 150, SHA – 105 and SHIO – 115. One out of every three prescriptions encountered per day were reviewed by the trained hospital pharmacists within the six months study period (Mid -June – Mid-December, 2013).

Data Collection tool - A standardized, validated data collection form known as the DRP-Registration Form V5.01 (PCNE Classification) was used by trained hospital pharmacists to document patients' data on identified drug therapy problems, causes and interventions by the trained pharmacists, the outcomes of these interventions and the doctors' acceptance rate. This form V5.01 distinguishes four domains: problems, causes, interventions and the corresponding outcome. Each domain also have sub-domains (see appendix 1) The version V5.01 was used in this study because it is simpler to use and a pilot study conducted earlier in Nigeria had demonstrated its effectiveness.[14]

Data Management - Data cleaning and double entry were done to ensure consistency of data generated. Data were presented as percentage frequencies, proportions and cross–tabulations using SPSS version 20.0.Summary statistics and statistically significant relationships between any of the dimension or domain

to determine the strength of the association were carried out.

Ethical Considerations - Ethical clearance for the study was obtained from the management of the hospitals. Informed consents of the participants in the study were also obtained and confidentiality of the information collected was ensured through maintenance of anonymity of patients' personal information.

RESULTS

The total number of prescriptions reviewed per hospital were: FMCA 15840, OOUTHS 6600, SHA 4620 and SHIO 5060. The tertiary hospitals had a larger flow of patients and also more DTPs with FMCA having the highest number of patients though OOUTHS had the higher no of DTPs per prescription (Table 1), however, there was no significant difference in the total number of prescriptions with DTP in either of secondary and tertiary hospitals in this study ($t_{(32118)}$=1.78, p=0.705).

Table 1 : Percentage prescriptions with DTPs in health facilities

Health facility	Prescriptions Reviewed	Prescriptions with DTPs	Prescriptions with DTPs (%)
FMCAA	15,840	53	0.33
OOUTHS	6,600	28	0.42
SHA	4,620	11	0.24
SHIO	5,060	12	0.23
TOTAL	32,120	104	0.32

The demographic distribution of encountered patients with DTPs in their prescriptions are presented in Table 2. Patients in age group 31-40yrs were the highest single category (24) while the age range 21- 60 constituted 76.92% of the total number of patients in all the health facilities and most of these patients were still from the tertiary hospitals. More female than male (64:38) sought care in the two categories of facilities studied.

Table 2: Demographic characteristics of patients with DTPs

Age range (yrs)	SHA	SHIO	Total (Secondary facility)	FMCAA	OOUTHS	Total (Tertiary facility)
0-10	2	1	3	5	0	5
11-20	0	1	1	0	0	0
21-30	1	7	8	4	5	9
31-40	3	1	4	18	2	20
41-50	2	1	3	12	5	17
51-60	1	0	1	6	12	18
61-70	0	0	0	4	2	6
0> 70	3	0	3	4	2	6
Total	12(11.54%)	11(10.57%)	23 (22.11%)	53(50.96%)	28(26.92%)	81(77.88%)
Male	5	5	10	22	10	32
Female	7	6	13	31	18	49

A total of 104 DTPs were reported in all the institutions: Drug Choice Problem (DCP) 35.59%, Dosing Problem (DP) 33.89, Adverse Drug Reaction (ADR) 22.88%, Drug Use Problem (DUP) 4.23%, and Drug Interaction (DI) 1.69% (Table 3).

DCPs were the major types of DTPs in all the centers 35.59%, with 57.15% being reported in the tertiary health facilities and 42.85% in secondary facilities. However, there was no significant difference between occurrence in the two hospital levels with $t_{(32118)} = 1.797$, $p = 0.073$.

With regards to occurrence of ADRs, there was a significant difference between the tertiary and secondary hospitals with $t_{(32118)} = 2.047$, $p = 0.041$.

Also testing for significance in the occurrence of DUPs between the two healthcare levels, there was no significant difference reported in the occurrence ($t_{(32118)} = 0.506$, $p = 0.613$); and same for DPs with $t_{(32118)} = 0.701$, $p = 0.483$; and for DI, $t_{(32118)} = 0.603$, $p = 0.546$

Table 3 : Types of DTPS in all health facilities

	ADR	DUP	DCP	DP	DI	Others	Total
	N	N	N	N	N	n	N
SHA	5	1	7	4	1	0	18
SHI	8	0	11	6	0	1	26
Total	13	1	18	10	1	1	44
FMCA	11	3	20	19	1	1	55
OOUTH	3	1	4	11	0	1	20
Total	14	4	24	30	1	1	74
Grand Total	27(22.88%)	5(4.23%)	42(35.59%)	40(33.89)	2(1.69)	2(1.69)	118(100%)

ADR = Adverse drug reactions, DUP = Drug Use Problem, DCP = Drug choice problem, DP = Dosing problem, DI = Drug Interactions, O = Others.

The occurrence of the various sub-groups of DTPs are presented in Table 4. Allergic reactions were reported more in tertiary health facilities (60%). Other subgroups of DTPs reported were: inappropriate drug/dosage, wrong drug taken/administered, drug dose too low, drug dose too high and treatment duration too long.

There was a significant difference in the occurrence of Non-allergic ADR in the two facility levels studied with $t_{(32118)}$=2.423, p=0.016 with a higher incidence of non-allergic ADRs at the secondary facilities. In the DCP subgroup, a significant difference was reported in the occurrence of duplication of drugs $t_{(32118)}$=2.153, p=0.032 with a higher incidence of duplications at the secondary hospital level. Similarly, a significant difference was also reported in the occurrence of contraindications between drugs and medical conditions with $t_{(32118)}$ =3.043, p=0.002, and a higher incidence of contraindications at the secondary level. There was no significant difference in the occurrence of inappropriate dosage forms $t_{(32118)}$=0.278, p=0.781.

In the DUP Subgroups, significant difference was only reported in the occurrence of longer than recommended dosing duration with a higher incidence among patients at the secondary hospitals ($t_{(32118)}$=2.387, p=0.017). No significant difference reported with Wrong drugs ($t_{(32118)}$=0.228, p=0.819) and Dose too low ($t_{(32118)}$=1.583, p= 0.114).

Table 4: Subgroups of DTPs reported in health facilities

DTP SUB GROUP	SHA	SHIO	Total Secondary	FMCA	OOUTHS	Total Tertiary
Adverse Drug Reaction Sub-group						
Side effect (non-allergic)	3	4	7(63.6%)	3	1	4(36.4%)
Side effect (allergic)	2	4	6(40.0%)	7	2	9(60%)
Drug Choice problem Sub- group						
Inappropriate drug/ form	3	8	11(32.4)	19	4	23(67.64%)
Duplication of drug (group)	2	0	2(100%)	0	0	0(0%)
Contraindication for Drug	1	3	4(100%)	0	0	0
Drug Use Problem Sub-Group						
No drug but clear Indication	0	0	0(0%)	0	0	0(0%)
Drug not taken /administered at all	0	0	0	1	0	1(100%)
Wrong drug taken /Administered	1	0	1(25%)	2	1	3(75%)
Drug dosing problem Sub-group						
Drug dose too low	1	0	1(10.0%)	5	4	9(90%)
Drug dose too high	3	0	3 (14.2%)	13	5	18 (85.8%)
Treatment duration Too short	0	0	0	0	0	0
Treatment duration too long	0	6	6(66.6%)	1	2	**3(33.3%)**

A total of 209 interventions were reported in all the facilities with 69 interventions at the secondary health level, comprising: 22 at prescriber level, 22 at patient/career level, 19 at drug level while 6 interventions were classified as others because they did not fit into the other categories (Table 5).

The tertiary institutions had a total of 140 interventions with 62 (44.28%) interventions at prescriber level, 27 (19.28%) at the level of patient/caregiver and 48 (34.28%) at drug level while only 3 interventions could not be categorized.

Interventions were recorded more at prescriber and drug levels in the tertiary health facilities while in the secondary facilities, interventions were more at prescriber and patient levels (31.88%). Drug changes were not as frequently made.

Table 5: Level of intervention steps for DTP resolution

Intervention	SHA	SHIO	TOTAL Secondary (%)	FMCA	OOUTHS	Total Tertiary (%)
No intervention	1	0	1(1.44)	0	0	0 (0.00)
Prescriber Level	14	8	22(26.20)	48	14	62(73.8)
Patient/Caregiver level	13	9	22(44.90)	21	6	27(45.1)
Drug Level	12	6	18(27.3)	34	14	48(72.7)
Others	1	5	6(66.6)	2	1	3(33.3)
Total	41	28	69	105	35	140

The overall outcome of intervention reported in the study are presented in Table 6. They include:problem totally solved (PTS), problem partially solved (PPS), problem not solved (PNS), lack of cooperation of patient (LOCOP) and outcome unknown (OOIU). Unknown outcome of intervention was documented more in the secondary health facilities (4), than in the tertiary hospitals ($t_{(89)}$=2.5783, $p<0.05$). Total resolution of DTPs was reported mainly in the tertiary facilities, constituting 77.22% of all the problems totally solved across the two categories of health facilities with statistically significant difference ($t_{(89)} = 2.678$, $p< 0.05$).

Table 6: Overall outcome of intervention in health facilities

	OOIU		PTS		PPS		PNS		LOCOP	
	n	%	n	%	n	%	n	%	n	%
SHA	2		12		0		0		0	
SHI	2		6		0		0		0	
Total (secondary	4	66.6	18	22.78	0	0	0	0	0	0
FMCA	2		44		6		0		0	
OOUTH	0		17		0		0		0	
Total	2	33.3	61	77.22	6	100	0	0	0	0
Overall total	6	100	79	100	6	100	0	0	0	0

OOIU = Outcome of intervention unknown, PTS = Problem totally solved, PPS = Problem partially solved, PNS = Problem not solved, LOCOP = Lack of cooperation of patient.

DISCUSSION

DTPs were reported in this study for both the secondary (General hospitals) and tertiary (Teaching Hospitals) health facilities. The tertiary hospitals had a larger number of patients visiting than the secondary facilities. The percentage occurrence of DTPs in the tertiary facilities were slightly higher but the differences were not significant. Type and frequencies of DTPs have been known to vary from one health facility level to another, from country to country and among different disease conditions within the same country.[15]

The mean age of respondents whose prescriptions had at least one DTP was 39.2±3.6 years and more female patients than male (64:38) had DTPs s on their prescriptions in the two categories of facilities studied. A study in Doha reported a mean age of 33±16.3years while similar findings of a large female: male ratio had been reported in Nigeria and Canada.[13, 14] The Canadian study had a population made up of 69% female with DTPs However, other studies in Nigeria and Europe have reported more DTPs among the male population, ranging from 52.3% - 64.7%.[15,16,17] The European study with 64.7% female population was carried out concurrently in 112 community pharmacies across 6 European countries: Austria, Denmark, Germany, The Netherlands, Portugal and Spain. The gender distribution may therefore be a function of study setting.

Drug choice problems (DCPs) were the major types of DTPs reported (35.59%) in this study for the two health levels with the bulk being reported in the tertiary facilities (57.15%) but this difference in documented DCPs between the secondary and tertiary facilities is not significant. DCP had been reported as the most frequently encountered type of DTPs (54%) in the prescription received in the pharmacy department of a primary healthcare facility in Doha, Qatar[18] and this DTP group was also the most frequently encountered category (36.8%) in prescriptions for a group of Type 2 Diabetes Mellitus patients. Other studies have however *reported* DCPs as the second most common DTP in community pharmacies.[19,20]

Occurrence of dosing problems in the tertiary health facilities, though higher but difference was not significant. This may just be a function of the large patient population being managed in the tertiary facilities. Occurrence of ADRs in the tertiary hospitals was however significantly higher with p=0.041. A study among diabetic patients reported ADR of 16.4% while 31.1% ADR was found in a study that focused on patients in general hospital setting.[15,21] The differences observed in the proportions recorded might have been due to factors associated with the patients' disease conditions.

DIs occurred in almost equal proportions in both the tertiary and secondary health facilities in this study with no significant difference. Some studies had reported DIs as the most frequently occurring DTP in a number of health settings. An occurrence of 36.9% was reported in a study among patients admitted to cardiology, geriatrics, respiratory and rheumatology wards, D1 occurred more (12.2%), in the cardiology patients.[21] DIs in community pharmacies in Switzerland were reported to be as high as 76%. Every pharmacy is equipped with software for D1 screening which is used to check every possible potential interaction even if not clinically relevant, hence the most frequently reported DTP were Drug interactions.[22]

The occurrence of drug use problems was very low (4.23%) in both tertiary and secondary facilities with no significant difference between the health levels. The broad category of 'others' accounted for 2.9% of DTPs encountered in this study. This includes patient dissatisfied with therapy 1.1 %, insufficient awareness of health and disease 1.1%, unclear complaints and further clarification necessary 0.6%. Another Nigerian study using the same documentation tool had reported 7.1% in this category of 'others' with only insufficient awareness of health and diseases as the only contributor.[14] The latter was carried out in a secondary facility without prior training for the pharmacists in the facility.

Non allergic ADR was more common in secondary facilities with a significant difference in occurrence. The most common subgroup in the drug choice category was 'inappropriate drug dosage' with 67.64% of total occurrence in the tertiary facilities but without a statistical difference. The secondary and tertiary hospitals work with a wider range of drugs and manage complex or chronic conditions. The doctors may therefore experiment with a considered inappropriate dosage in the management process. Patients may even be given personalized dosages. Dose-related problems had been reported as the most frequently encountered cause of drug related problems in general hospitals in Norway while drug under dose/low dose was one of the most common DTPs in elderly patients.[22,23]

Intervention steps were taken to resolve DTPs and outcome categorized. The intervention with outcome unknown was statistically higher in the secondary health facilities (66.6%) than the tertiary. By contrast, a significantly higher number of the DTPs were totally resolved in the tertiary facilities. The higher resolution in tertiary facilities may be a function of the level of

expertise and experience of the doctors and pharmacists practicing in the hospitals. The level of DTP resolution confirms that collaboration between physicians and pharmacists improve patient care outcome. The total number of interventions made by pharmacists was 209, averaging approximately 2 interventions per prescription. At prescriber level, intervention proposed and approved by prescriber (IPABP) was 77% implying a 77% acceptance rate of the recommendation of hospital pharmacists by the physicians. A study on neurology in-patients reported an acceptance of 62% while acceptance rate as high as 83% was reported for general medical hospital in-patients unit and 93% for out-patients attending a specialist hypertensive clinic.[24,25] A strategy by which recommendations to prescribers should be restricted to those with the highest clinical relevance and most likely benefit have been suggested. It is important to provide physicians with choices, so that their sense of freedom is maintained. It is envisaged that this will improve acceptance rate of interventions.[26] Such patient-oriented pharmacy practice in Nigerian hospitals is limited by inadequate infrastructure, lack of relevant training for pharmacists, resistance of physicians to ward activities by pharmacists and lack of self-confidence on the part of pharmacists.[27,28] Low density of pharmacists is also a militating factor, Nigeria has only 10 pharmacists for 100,000 people, compared to minimum of 50:100,000 recommended by WHO.[29] Though acceptance of intervention is increasing, there is an urgent need to enhance the capacity of pharmacists through adequate training to boost knowledge and self-confidence which should translate into the optimization of patient therapy outcomes.

This study however had some limitations: The number of interventions reported is perhaps not a fair reflection of the actual number of DTPs in the clinics because the study did not consider prescriptions contained in the in-patient case notes. The pharmacists are not part of the team of health workers that conduct clinical ward-rounds.

CONCLUSION

Drug therapy problems occurred throughout the drug use processes in the secondary and tertiary health care settings but without significant difference in the volume of occurrence in the two health levels. The most common categories of DTPs were drug choice problem, with significant differences in occurrence of contraindications and duplication of drugs, both occurring more in secondary facilities. Adverse drug reactions also occurred more in secondary facilities. No significant difference in occurrence of dosing problems, drug interactions and drug use problems. The study reported the vital role of Pharmacists in identifying, preventing and resolving DTPs for the optimization of patient care outcomes. Physicians' acceptance of pharmacists' recommendations was quite high and patients counseling and referral to prescriber were effective tools of intervention for the resolution and prevention of DTPs. The impact of Pharmacists intervention in significant positive patient outcomes revealed the multidisciplinary approach required in the management of DTP and the need for improvement in medication reviews, documentation and collaboration with physicians as part of routine activities of pharmacists in relevant pharmacy practice settings.

ACKNOWLEDGEMENT – This study was funded through a research grant awarded by the Board of Fellows of the Pharmaceutical Society of Nigeria. The authors therefore wish to acknowledge this financial support. We also appreciate the management and staff of the health facilities for their cooperation in the course of the study.

REFERENCES

1. Oparah AC (2010). Essentials of Pharmaceutical Care, pp 83-92. Lagos: All Deals Inv. Co. Ltd.
2. Viktil, K.K., Blix, H..S,Moger, T.A and Reikvam,.A,,(2006). Interview of patients by pharmacists contributes significantly to the identification of drug-related problems (DRPs). *Pharmacoepidemiology of Drug Saf*ety; 15(9): p. 667-74.
3. Hammerlein, A., N. Griese, and M. Schulz,(2007). Survey of drug-related problems identified by community pharmacies. *Annals of Pharmacother*apy; 41(11): p. 1825-32.
4. Krahenbuhl-Melcher, A.,(2007). Drug-related problems in hospitals: a review of the recent literature. *Drug Saf*ety; 30(5): p. 379-407.
5. Lampert, M.L., S. Kraehenbuehl, and B.L. Hug,(2008). Drug-related problems: evaluation of a classification system in the daily practice of a Swiss University Hospital. *Pharmacy World and Science;* 30(6): p. 768-76.
6. Gillespie U, Alassaad A, Henrohn D, Garmo H, Hammarlund-Udenaes M, Toss H,(2009).A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. *Archives of Internal*

Medicine; 11;169(9):894-900.

7. Berthouzoz S, Berger L, Bonnabry P and Pannatier A (2012). The hospital pharmacist: An important contributor to improved patient safety in the hospital. *Chimia (Aarau);* 66: 300- 303.
8. Manno, M.S and Hayes, D.D.(2006). Best-practice interventions: how medication reconciliation saves lives. *Nursing*. ;36(3):63-4.
9. Makowsky, M.J, Koshman, S.L, Midodzi, W.,K and Tsuyuki, R.T.(2009); Capturing outcomes of clinical activities performed by a rounding pharmacist practicing in a team environment: the collaborate study [NCT00351676]. *Med Care*. 47(6):642-50.
10. Hellstrom LM, Bondesson A, Hoglund P, Midlov P, Holmdahl L and Rickhag E (2011). The impact of the Lund Integrated Medicines Management (LIMM) model on medication appropriateness and drug-related hospital revisits. European Journal of Clinical Pharmacology; 67 (7): 741 - 752.
11. Lisby M, Thomsen A, Nielsen LP, Lyhne NM, Breum-Leer C and Fredberg U (2010). The effect of systematic medication review in elderly patients admitted to an acute ward of internal medicine. Basic Clinical Pharmacology and Toxicology; 106 (5): 422 - 427.
12. Stemer G and Lemmens-Gruber R (2011). The clinical pharmacist's contributions within the multidisciplinary patient care team of an intern nephrology ward. International Journal of Clinical Pharmacy; 344 (5): 678 – 683.
13. Foppe VM,(2005). Effectiveness of interventions by community pharmacists to improve patient adherence to chronic medication: a systematic review. Annals of Pharmacotherapy 39(2): p. 319-28. 127
14. Bakare M, Oreagba AI and Adeniran B (2011). Drug therapy problems: pharmacists´ interventions and outcomes in Lagos state general hospitals, South West, Nigeria. West African Postgraduate College of Pharmacists (Nigerian Chapter) Newsletter; 1 (4): 10. 29.
15. Odili VU, Egiebor BO, Oparah AC.Identification of drug therapy problems in patients with diabetes treated in a secondary care facility in Benin City. Nat J Trop Research, 2011; 9(1) 72-81. 30
16. Uchenna IH Eze and Adebiyi O Olowu, Prescribing Patterns and Inappropriate Use of Medications in Elderly Outpatients in a Tertiary Hospital in Nigeria *Tropical Journal of Pharmaceutical Research* February 2011; 10 (1): 19-25
17. Nickerson A, MacKinnon NJ, Roberts N and Saulnier L (2005).Drug-Therapy Problems, Inconsistencies and Omissions Identified During a Medication Reconciliation and Seamless Care Service. Healthcare Quarterly; 8: 65 - 72.
18. Nadir Kheir, Zaidan Manal, Younes Husam, El Hajj Maguy, Wilbur Kerry, Jewesson Peter J. Pharmacy education and practice in 13 Middle Eastern countries. Am J Pharm Educ. 2008;72(6):133. http://ukpmc.ac.uk
19 Binu KM, Nimmy N John, and Geo P Varghese. (2012) A Survey Of Drug Related Problems Identified By Community Pharmacy In South India *International Journal Of Pharmaceutical, Chemical And Biological Sciences*, 2(2), 369-374
20 Patrick E., Manuel H., Markens L., Kurt E. and Heberger (2010) Provision of Pharmaceutical Care by Community Pharmacists. *Pharmacy World and Science;*20:(4)53-60.
21 Blix HS, Viktil KK, Reikvam A, Moger TA, Hjemaas BJ and PretschP (2004). The majority of hospitalised patients have drug-related problems: results from a prospective study in general hospitals. *European Journal of Clinical Pharmacology;* 60(9):651– 658
22 Paulino, E.I, Bouvy, M.L, Gastelurrutia, M.A, Guerreiro M and Buurma, H.(2004). Drug related problems identified by European community pharmacists in patients discharged from hospital. *Pharmacy World and Sci*ence ;26:(3)53-60.
23 Rao D, Gilbert A , Strand L, Cipolle R, 2007, Drug therapy problems found in ambulatory patient populations in Minnesota and South Australia *Pharm World Sci*; 29:647 – 654
24. Holland, R, Battersby, J, Harvey, I, Lenaghan, E, Smith, J and Hay, L.(2005).Systematic review of multidisciplinary interventions in heart failure. *Heart.*;91(7):899-906.
25. Spinewine ,A, Swine, C, Dhillon, S, Lambert,P, Nachega, J.B and Wilmotte, L.(2007). Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial. *Journal of American Geriatrics Society*;55(5):658-65.58
26. deAlmeida SM, Gama CS and Akamine N (2007). Prevalence and classification of drug-drug interactions in intensive care patients: Einstein; 5(4): 347-35129.

27. Erah PO, Nwazuoke JC (2002) Identification of standards for pharmaceutical care in Benin City. Trop J Pharm Res 1(2):55-66
28. Joda AE, Nwaokomah SO (2011) Assessment of pharmacy students' willingness to practice after graduation. West African J Pharm 22(1):82-90