

Full Length Research paper

Impact of pharmaceutical performance through interventions by pharmacy

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The study aimed to identify and analyze drug-related problems (DRP), negative outcomes associated with medication (NOM) and the impact of pharmaceutical performance through interventions by pharmacy residents at the University Hospital of Campo Grande, Mato Grosso do Sul, Brazil. This retrospective, cross-sectional single-center study analyzed data registered in Pharmaceutical Intervention forms recorded by pharmacy residents between March 2011 and February 2012. DRP and NOM were classified according to the definitions proposed by the Third Consensus of Granada (2007). A total of 256 pharmaceutical interventions from 155 patients were registered, of which 50.78% were from patients of 60 years of age or above. Majority of interventions took place in the surgery wards, medical clinic and adult intensive care unit, with 89.06% of interventions being accepted. Among these interventions, 401 DRP, of which 21.07% were related to the probability of adverse effects, and 298 NOM, of which 33.87% were related to non-quantitative safety problems, were observed. Anti-infectives for systemic use were shown to be the group most often involved with DRP. Treatment effectiveness was the reason for intervention in 80.23% of forms. A close relationship between physicians and pharmacists ensures more rapid identification of prescription errors, possible adverse effects, DRP and NOM. Despite of the issue importance, the published studies on the topic remains scarce. The results of studies that evaluate DRP and NOM collaborate with the analysis of the pharmaceutical service provided to hospitalized patients in the present study.

Key words: Drug-related problems, negative outcomes associated with medication, pharmacotherapeutic monitoring, hospital pharmaceutical care, third consensus of Granada.

INTRODUCTION

According to Hepler and Strand (1990), the practice of pharmaceutical care involves the pharmacist's participation in healthcare interventions, including pharmaceutical

interventions (PhI). This conduct is characterized as a planned, documented act involving the user and health professionals, which aims to solve or prevent issues that

may interfere with pharmacotherapy and is included as part of the monitoring of the pharmacotherapeutic process (OPAS, 2002).

Several studies have shown that the participation of the pharmacist in reviewing patient pharmacotherapy can result in significant reduction in drug-related problems (DRP), negative outcomes associated with medication (NOM), patient length of stay, and treatment costs (Conde et al., 2006; Gandhi et al., 2001; García et al., 2002; Soria et al., 2011). DRP pertains to situations in which the medication use process may cause a negative result, while NOM refer to inadequate results from these situations related to medication use (Comitê de Consenso, 2007).

The main objectives of therapeutic monitoring include ensuring the rational and proper use of drugs to achieve the desired pharmacotherapeutic outcomes, maximizing the beneficial effects of drugs, preventing or minimizing undesirable effects and promoting collaboration for the reduction of spending on patient care (Farré Riba et al., 2000). In order to prevent errors or prevent errors from reaching the patient, the healthcare team's performance must be effective. Healthcare professionals should perform in an integrated manner during the steps of selection, management, prescription, dispensation, administration of drugs and post-administration monitoring (Nunes et al., 2008).

Thus, this study aimed to identify and analyze DRP, NOM, and the impact of pharmaceutical performance through interventions by pharmacy residents at the University Hospital of Campo Grande in the state of Mato Grosso do Sul, Brazil.

METHODOLOGY

Design, setting and subjects

This single-center, retrospective cross-sectional study was conducted at the Maria Aparecida Pedrossian University Hospital Center of the Federal University of Mato Grosso do Sul (NHU/UFMS). It is a tertiary teaching hospital with 280 bed capacity and a member of the Brazilian Unified Health System (Sistema Único de Saúde - SUS).

There was no selection of subjects. The NHU/UFMS pharmacy residents registered all pharmaceutical interventions performed in a specific form developed by the hospital pharmacy service during the study period.

Data collection

The analysis of DRP, NOM and the impact on pharmaceutical performance was based on information registered in Pharmaceutical Intervention forms completed by five pharmacy residents from March 2011 to February 2012.

Data on patient gender, age group and hospital sector of admission were recorded in the form. Data exposed in Table 1 were also registered. In addition to intervention result, a summary of the intervention performed and the results of the intervention were recorded. These data were used as a base to identify DRP and

NOM, according to the proposal of the Third Consensus of Granada (Comitê de Consenso, 2007).

Multiple causes were accepted in data collection, as the patient may have been subjected to more than one DRP. The DRP related to personal characteristics of the patient included any impediment the patient may have presented due to the administration of any medication, that is, allergies, ideological/religious beliefs and/or refusal of treatment. The classification "other" was defined by the authors of this study as interventions related to prescription confirmation, change of prescribed drug formulation and replacement of a non-standardized drug for a standardized drug in the hospital's pharmacotherapeutic guide.

After identifying the DRP and NOM and conducting the intervention, the process was evaluated by the application of the adapted pharmaceutical performance impact code proposed by Farré Riba et al. (2000) (Table 2).

Statistical analysis

Data was stored in Excel® 7.0 spreadsheets and statistical analyses were performed using Epi Info 3.5.1 (CDC, Atlanta, Georgia, USA). Results were presented in tables and included the description of absolute and relative frequency.

RESULTS

During the study period, 256 pharmaceutical interventions involving 155 patients were registered. Patients aged 60 years or older and male patients were involved in 50.78 and 51.56% of pharmaceutical interventions, respectively, while the young adult (17 to 29 years of age) age group underwent fewer interventions (8.30%) (Figure 1).

Most interventions took place in the Surgical Clinic Wards, Clinic Wards, and Adult Intensive Care Unit. The remainder hospital sectors had a lower rate of care, particularly the Maternity Ward which only performed two interventions for one patient (Table 3). The pharmaceutical interventions were mainly active, drug related, communicated verbally, had the physician as interlocutor and were accepted. Interventions that were not accepted mainly involved the indication for treatment initiation, suggestion of exchange and/or reduction of antimicrobial agent dose and dilution of drugs, most notably fentanyl, tramadol and amphotericin B deoxycholate.

Table 4 shows the distribution of DRP and NOM by hospital sectors. In interventions related to drugs (193/256), 401 DRP were identified, with an average of 1.60 ± 1.189 SD (minimum zero and maximum five) DRP per patient attended. Most frequent DRP were the likelihood of adverse effects and inadequate specified strength, dose and/or treatment length. For NOM, 248 events were observed, with an average of 1.0 ± 0.724 SD (minimum zero and maximum three) NOM per patient. Most frequent NOM were non-quantitative safety issues and untreated health issues.

Drugs related to DRP were classified using levels 1 and 2 of the Anatomical Therapeutic Chemical (ATC) classification

Table 1. Pharmaceutical interventions (PhI).

Form of detection	Active: when the pharmacy resident was the first professional to find the problem Passive: when the pharmacy resident was alerted by any other professional about a possible existing problem
Type	Related to medications taken Not related to medications taken
Interlocutor	Physician or nursing staff Other health professionals
Form of communication	Verbal Written Verbal and written
Intervention result	Accepted: change in the conduct of the interlocutor involved up to 72 hours after the PhI, Not accepted: interlocutor does not change their behavior within 72 hours after the PhI or non-responsive PhI.

Table 2. Pharmaceutical performance impact code (Farré Riba et al., 2000).

Optimization of pharmacological treatment (effectiveness)	
Indication	Indicate drug Discontinue drug Change to more effective drug
Dosage	Change treatment duration Change equivalent strength/interval of dosage
Route	Change to a more effective route Recommend the administration method
Preventive pharmaceutical interventions (toxicity)	
Adverse effects	Prevent allergic reaction Prevent adverse effects
Interactions	Confirm prescription Prevent pharmacological interaction
Route	Change to a safer route

system (WHO, 2012) and the main group involved in interventions was anti-infectives for systemic use. For the most frequent subgroup, classification was extended up to level 3 and the main subgroup was anti-bacterial for systemic use, most notably glycopeptides (Table 5).

The impact code (Table 6) was applied only in accepted pharmaceutical interventions related to drugs. Of these, 80.23% addressed the effectiveness of treatment, while 19.77% were preventive interventions for toxicity. Most interventions for effectiveness aimed at changing the specified strength or interval, while

interventions related to toxicity were focused on confirming the prescription.

DISCUSSION

The high acceptance of pharmaceutical interventions shows pharmacists can perform effectively in patient care by taking responsibility for pharmacotherapy, ensuring compliance with the established treatment plan and

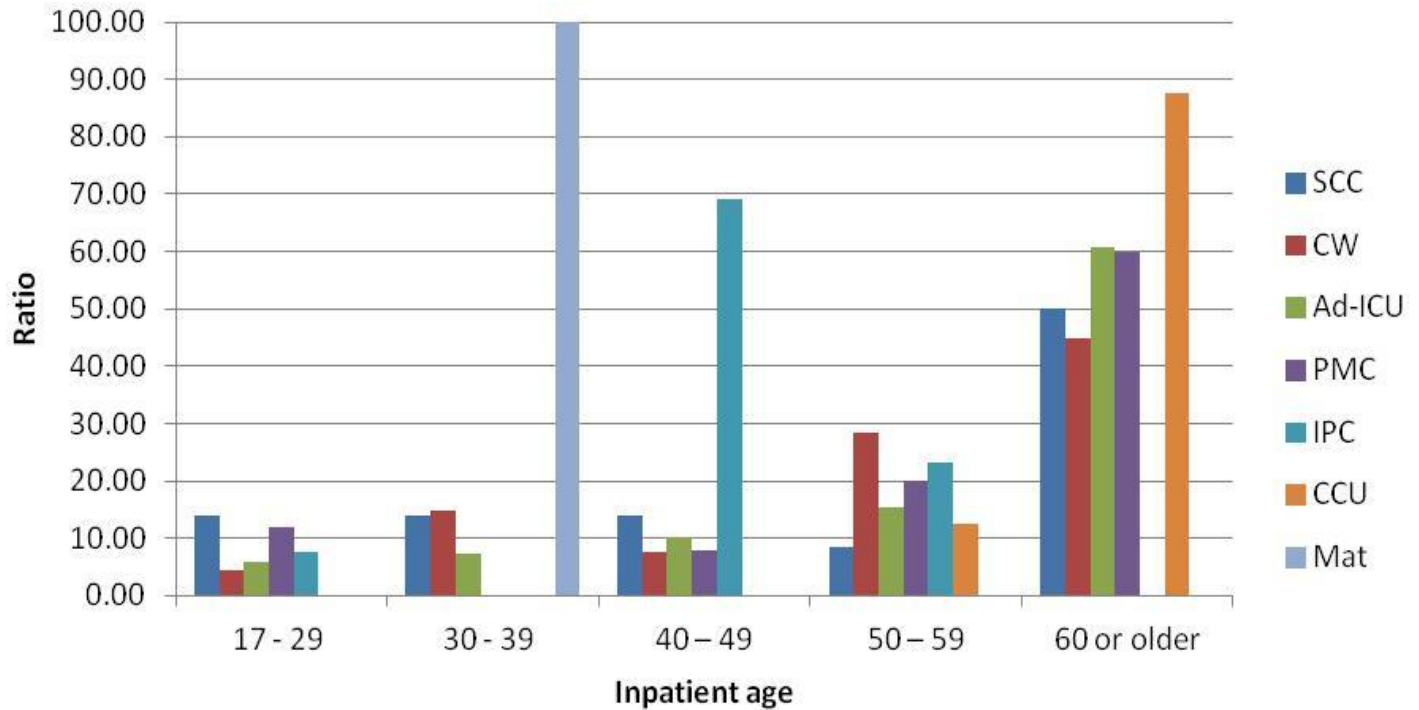


Figure 1. Age distribution of inpatients involved in 256 interventions according to the hospital sector. SCC: Surgical Clinic Wards; CW: Clinical Wards; Ad-ICU: Adult Intensive Care Unit; PMC: Prompt Medical Care; IPC: Infectious and Parasitic Disease; CCU: Coronary Care Unit; MAT: Maternity.

Table 3. Distribution of pharmaceutical interventions according to clinical.

Phi	SCC (%)	CW (%)	Ad-ICU (%)	PMC (%)	IPC (%)	CCU (%)	MAT (%)	Total	
								n	%
Detection	28.13	26.17	26.95	9.77	5.08	3.13	0.78	256	100
Active	72.22	80.60	84.06	84.00	38.46	87.50	50.00	198	77.34
Passive	27.78	19.40	15.94	16.00	61.54	12.50	50.00	58	22.66
Type	28.13	26.17	26.95	9.77	5.08	3.13	0.78	256	100
Drug related	59.72	80.6	79.71	88.00	84.61	75.00	100.0	193	75.39
Not drug related	40.28	19.4	20.29	12.00	15.39	25.00	-	63	24.61
Contact	28.13	26.17	26.95	9.77	5.08	3.13	0.78	256	100
Verbal	100.0	95.53	97.10	96.00	84.61	100.0	-	246	96.09
Other	-	4.47	2.90	4.00	15.39	-	100.00	10	3.91
Interlocutor	28.13	26.17	26.95	9.77	5.08	3.13	0.78	256	100
Physician	83.33	89.55	98.55	100.0	84.62	100.0	50.00	233	91.02
Other	16.67	10.45	1.45	-	15.38	-	50.00	23	8.99
Result	28.13	26.17	26.95	9.77	5.08	3.13	0.78	256	100
Accepted	81.94	89.55	91.30	92.00	100.0	100.0	100.0	228	89.06
Not accepted	18.06	10.45	8.70	8.00	-	-	-	28	10.94

SCC: Surgical Clinic Wards; CW: Clinical Wards; Ad-ICU: Adult Intensive Care Unit; PMC: Prompt Medical Care; IPC: Infectious and Parasitic Disease; CCU: Coronary Care Unit; MAT: Maternity.

Table 4. Distribution of DRP and NOM identified in pharmaceutical interventions.

Distribution	SCC	CW	Ad-ICU	PMC	IPC	CCU	MAT	Total	
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	n	%
DRP	19.70	26.18	30.67	9.98	9.23	3.74	0.50	401	100
Incorrect drug administration	0.75	2.49	3.99	0.75	2.00	0	0	40	9.98
Personal patient characteristics	0.25	0.50	0.25	0.25	0.25	0	0	6	1.50
Improper storage	0.25	0	0	0	0.25	0	0	2	0.50
Contraindication	0.25	0	0	0	0.50	0	0	3	0.75
ISDTD	4.49	4.99	6.73	2.24	1.50	0.75	0	83	20.70
Duplicity	0.50	0	0.50	0	0	0	0	4	1.00
Non-compliance with protocols	0.50	0	0	0	0.25	0.25	0	4	1.00
Drug interactions	1.25	0.25	2.24	0.50	0.75	0	0.25	21	5.24
Other health issues affecting treatment	0.50	2.74	1.75	0.25	0.50	0.50	0	25	6.23
Likelihood of adverse effects	4.24	4.74	7.98	1.75	2.00	0.75	0.25	87	21.70
Insufficiently treated health	4.74	6.98	2.99	2.49	0.25	1	0	74	18.45
Other	2.00	3.49	4.24	1.75	1.00	0.50	0	52	12.97
NOM	22.98	28.23	29.44	10.08	6.05	2.82	0.40	248	100
Untreated health issue	6.45	10.89	5.65	3.63	0.40	0.81	0	69	27.82
Effect of unnecessary drug	3.63	3.63	2.82	0.40	0.81	0.40	0	29	11.69
Non-quantitative ineffectiveness	2.02	2.42	4.03	1.61	1.21	0	0	28	11.29
Quantitative ineffectiveness	3.23	2.82	2.42	0	0	0.40	0	22	8.87
Non-quantitative safety issue	5.24	6.05	13.71	4.44	3.23	0.81	0.40	84	33.87
Quantitative safety issue	2.42	2.42	0.81	0	0.40	0.40	0	16	6.45

SCC: Surgical Clinic Wards; CW: Clinical Wards; Ad-ICU: Adult Intensive Care Unit; PMC: Prompt Medical Care; IPC: Infectious and Parasitic Disease; CCU: Coronary Care Unit; MAT: Maternity; ISDTD: Inadequate specified strength, dose and/or treatment duration.

preventing the occurrence of DRP and NOM. Most patients were aged 60 years or above, a characteristic that was also found in studies conducted by Al-Hajje et al. (2012), Jiang et al. (2012) and López et al. (2011). Elderly patients are known to be more vulnerable to DRP due to age-related physiological changes that may change pharmacokinetics and pharmacodynamic properties of drugs and frequent comorbidities that require the prescription of multiple drugs (Chan et al., 2012). These factors generate polypharmacy, which is one of the major determinants of many DRP aspects, such as adverse drug events, drug interactions and inappropriate drug selection (Chan et al., 2012; Elliot et al., 2012; Hanlon et al., 2004).

The hospital sector in which most interventions took place was the Adult Intensive Care Unit. In addition to greater interaction among pharmacists and other members of the healthcare team, the greater number of interventions in this clinic is justified by the characteristics of hospitalized patients, which comprise a greater number of related diseases and comorbidities, medication use, procedures and technologies, generating higher possibilities of pharmaceutical performance.

The pharmacy residents focused their activities in surgical clinics, medical clinic, infectious and parasitic disease clinic, prompt medical care, adult intensive care unit, and coronary care unit. Their participation in the

related clinics of pediatric patients and maternity took place solely when requested for advice, thus justifying the few interventions taking place at maternity hospital.

Farrell et al. (2012) stated that a pharmacist who directly performs patient care tends to be more capable of initiating case discussions with physicians, conducting their own patient interview and even managing a multidisciplinary team. Also, the presence of the clinical pharmacist increases their contact with other healthcare professionals and allows for verbal interventions, as observed in this study.

Monitoring of patients conducted by the pharmacists enables them to make interventions in different areas of their duties. While the focus on medication related interventions was very clear, interventions not related to medications was divided into two parts. One of these parts involved performing biochemical and microbiological laboratory tests, which aided in the monitoring of patient clinical status and directing specific antibiotic therapy. This practice contributes to the rational use of antimicrobial agents and prevents the appearance of multi-resistant microorganisms. The other part was related to filling out specific documentation for dispensing medications, ensuring that the patient was given all drugs prescribed.

Pharmaceutical interventions should be documented in the patient medical record. However, this was rarely

Table 5. Therapeutic groups related to DRP identified in pharmaceutical interventions classified according to the Anatomical Therapeutic Chemical (ATC).

ATC	Therapeutic group levels 1 (N>10) and 2	N	%
A	Alimentary tract and metabolism	34	13.28
A.02	Drugs for acid disorders	22	8.59
B	Blood and blood forming organs	17	6.64
B.05	Blood substitutes and perfusion solutions	8	3.13
C	Cardiovascular system	33	12.89
C.09	Agents acting on the renin-angiotensin system	14	5.47
J	Anti-infectives for systemic use	122	47.66
J.01	Anti-bacterial for systemic use	92	35.94
J.02	Anti-mycotics for systemic use	30	11.72
N	Nervous system	31	12.11
N.02	Painkillers	10	3.91
N.03	Anti-epileptic	10	3.91
ATC	Therapeutic group among anti-infectives for systemic use level 3 (N≥ 5)	N	%
J.01.XA	Glycopeptides	37	40.22
J.01.DD	3rd generation cephalosporins	8	8.70
J.01.XB	Polymyxins	8	8.70
J.01.DH	Carbapenems	7	7.61
J.01.MA	Fluoroquilolones	7	7.61
J.01.XX	Oxazolidinones	5	5.43

observed in the present study. Only 10 cases had written interventions, four of them being medical records and six of them being registers in the prescription itself. This result can be explained in part by the newly instated practice of pharmacists making notes in medical records, added to the residents' lack of experience in documenting their actions. Another possible factor may be due to the resistance of professionals in registering pharmaceutical interventions in the patient record.

The professional involvement of physicians with the interlocutor of pharmaceutical interventions has already been demonstrated in other studies (Conce et al., 2006; Nunes et al., 2008; Torner et al., 2003). A close relationship between physicians and pharmacists ensures more rapid identification of prescription errors, possible adverse effects, DRP and NOM.

An 80% acceptance rate for pharmaceutical interventions was also noted in several studies (Al-Hajje et al., 2012; Arroyo et al., 2009; Conde et al., 2006; Soria et al., 2011; Torner et al., 2003). A study conducted by López et al. (2011) described a 100% acceptance rate. Significant acceptance rate values, such as the one found in this study, illustrate the role of the clinical pharmacists in ensuring compliance with the pharmacotherapeutic goals set by each patient. The reduction of antimicrobial specified strength was the target of unaccepted interventions in this study.

Inadequate specified strength, dosage and/or treatment duration (ISDTD) and probability of adverse effects (PAE)

were the most frequently encountered DRP. This may occur because the study was conducted in a teaching hospital and most prescribers are resident doctors.

For a population similar to the one analyzed in this study, the group of drugs most associated with DRP was also the anti-infectives for systemic use (Arroyo et al., 2009; Conde et al., 2006; Farré Riba et al., 2000). The greater involvement of subgroup J.01.AX (glycopeptides) occurred due to frequent interventions in the adjustment of teicoplanin specified strength after three days of using double specified strength as the loading dose.

The impact code indicates the intervention rational and the benefit generated by the attention to patient regarding treatment effectiveness and/or toxicity. Pharmaceutical interventions enabling the optimization of pharmacological treatment provided to the patient influence the effectiveness. Effectiveness is considered to increase in events where intervention is motivated by subdosing, treatment omissions, improper drug selection, administration route or mode decreasing effectiveness, lack of treatment monitoring or existence of interactions impairing its effectiveness. Preventive pharmaceutical interventions enabling the risk reduction of medication use by the patient can lessen toxicity. Such risk is considered to exist if an intervention is motivated by overdosing, use of non-indicated drugs, modification of administration route to a safer one, detection of adverse reactions, allergies, interactions and prescription errors (Farré Riba et al., 2000).

Table 6. Impact of accepted pharmaceutical interventions.

Optimization of pharmacological treatment (effectiveness)	N (142)	% (80.23)
Indication	69	38.98
Indicate drug	31	17.51
Discontinue drug	17	9.60
Change to a more effective drug	21	11.86
Dose	55	31.07
Change specified strength/interval	53	29.94
Change treatment length	2	1.13
Route	18	10.17
Change to a more effective route	6	3.39
Recommend the administration method	12	6.78
Preventive pharmaceutical interventions (toxicity)	35	19.77
Adverse effects	19	10.73
Prevent allergic reaction	1	0.56
Prevent adverse effects	3	1.69
Confirm prescription	15	8.47
Interactions	8	4.52
Prevent drug interaction	8	4.52
Route	8	4.52
Change to a safer route	8	4.52

Despite the positive results presented here, in order to achieve a better analysis of the hospital pharmaceutical care service, issues such as cost reduction to the institution, hospitalized patient satisfaction and clinical outcome should be evaluated as well.

Conflict of interest

The authors declare no conflicts of interest.

REFERENCES

- Al-Hajje AH, Atoui F, Awada S, Rachidi S, Zein S, Salameh P (2012). Drug-related problems identified by clinical pharmacist's students and pharmacist's interventions. *Ann. Pharm. Fr.* 70:169-76.
- Arroyo LA, Grana EC, Ros NB, Meroño SR, Gil MP, Baines JPO, Payá JS (2009). Evaluación de un programa de intervención farmacéutica en pacientes con medicamentos de riesgo renal. *Farm. Hosp.* 33(3):147-54.
- Chan DC, Chen JH, Kuo HK, We CJ, Lu IS, Chiu LS, Wu SC (2012). Drug-related problems (DRPs) identified from geriatric medication safety review clinics. *Arch. Gerontol. Geriatr.* 54(1):168-74.
- Comité de Consenso (2007). Tercer Consenso de Granada sobre Problemas Relacionados con Medicamentos (PRM) y Resultados Negativos Asociados a la Medicación (RNM). *Ars. Pharm.* 48:5-17.
- Conde CA, Aquerreta I, Eslava AO, Zamarbide OG, Deiró JG (2006). Impacto clínico y económico de la incorporación del farmacéutico residente en el equipo asistencial. *Farm. Hosp.* 30:147-54.
- Elliot RA, Martinac G, Campbell S, Thorn J, Woodward MC (2012). Pharmacist- led medication review to identify medication-related problems in older people referred to an aged care assessment team: a randomizes comparative study. *Drugs Aging* 29:593-605.
- Farré Riba R, Clópes Estela A, Sala Esteban M, Castro Cels, I, Gámez Lechuga M, López Sánchez S, Tomás Sanz R. Alba Aranda G, Castillo Álvarez F, García Peláez M, Montejo Arcusa O, Serra Soler G, Sanz Mazó M (2000). Intervenciones farmacéuticas (parte I): metodología y evaluación. *Farm. Hosp.* 24(3):136-44.
- Farrell B, Ward N, Dore N, Russel G, Geneau R, Evans S (2012). Working in interprofessional primary health care teams: what do pharmacists do? *Res. Social Adm. Pharm.* 1:1-14.
- Gandhi PJ, Smith BS, Tataronis GR, Maas B (2001). Impact of a pharmacist on drug cost in a coronary care unit. *Am. J. Health-Syst. Pharm.* 55:497-503.
- García NI, Jané CC, Creus MT, Dalmau LM, Vila RG, Sala JR (2002). Evaluación de la integración del farmacéutico em equipos de atención de unidades de hospitalización. *Farm. Hosp.* 24:18-27.
- Hanlon JT, Lindblad CI, Gray SL (2004). Can clinical pharmacy services have a positive impact on drug-related problems and health outcomes in community-based older adults? *Am. J. Geriatr. Pharmacother.* 2:3-13.
- Hepler CD, Strand LM (1990). Opportunities and responsibilities in pharmaceutical care. *Am. J. Hosp. Pharm.* 47:533-43.
- Jiang SP, Zheng X, Li X, Lu XY (2012). Effectiveness of pharmaceutical care in an intensive care unit from China: a pre- and post-intervention study. *Saudi Med. J.* 33:756-62.
- López IM, Pazo -Oubiña F, Vilardell PL (2011). Atención farmacéutica integral a los pacientes de um servicio de Cirugía Vasculat. *Farm. Hosp.* 35:260-3.
- Nunes PHC, Pereira BMG, Nominato JCS, Albuquerque EM, Silva LFN, Castro IRS, Castilho SR (2008). Intervenções farmacéuticas e prevenção de efeitos adversos. *Rev. Bras. Ciênc. Farm.* 44(4):691-9.
- Organização Panamericana De Saúde (OPAS) (2002). Consenso brasileiro de atenção farmacéutica: proposta. *Atenção Farmacéutica no Brasil: Trilhando Caminhos.* Brasília, Organização Pan-Americana da Saúde.
- Soria MALM, Marti MC, Torres NVJ (2011). Aceptación de recomendaciones en el paciente con oportunidades de mejora farmacoterapéutica. *Farm. Hosp.* 35:51-7.
- Torner MQG, Estradé EO, Solernou FP (2003). Atención farmacéutica en lós problemas relacionados com lós medicamentos em enfermos hospitalizados. *Farm. Hosp.* 27:280-89.
- World Health Organization (WHO) (2012) . Anatomical Therapeutic Chemical Classification (ATC Code), 2012. Available at: <<http://www.whocc.no/atcddd>> Accessed 21st August 2012.