



Reporting of Medication Errors by Pharmacist in the Treatment of Chronic Kidney Failure in Tertiary Hospital Peshawar

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ABSTRACT

Medication error is any avoidable practice that may direct to harm the patients or increase cost on patient directly or indirectly. While prescribing, dispensing or administering medication to patient any mistake may lead to harm the patients. The practice of medication error is most common in developing countries including Pakistan. The present study was carried out to analyze different type of medication errors during prescribing, dispensing or during administration of drugs and to find out the measure for the control of these error in order to save the life of general population or to decrease hospitalization or to decrease cost on patients. The aim of study was also to find the prevalence of medication errors & promote safety in use of medication by ensuring effective utilization of pharmacist in ward setting. The present study was conducted in the nephrology ward of 500- bed multidisciplinary tertiary hospital located at Peshawar Kpk. It was prospective study in which 60 patients histories were analyze for medication related error and then reported by pharmacist in nephrology ward. Data from each patient were collected through special profarma which include demographic of patients, medication record, dosage form of medication, previous medication record, previous surgical history, adverse reaction, medication error, any drug interaction. Then after collecting data of each patient were evaluated for rational therapy and any medications related error analyze were then reported in order to prevent the reoccurrence of such error. In this study population of n= 60 (female 39 & male 21). Female were more prone to chronic kidney failure. CKD ratio was found greater in age of 40-60 year. Diabetic mellitus and hypertension were the two main risk factors associated with CKD the ratio of which was 20% and 53.33% respectively. Total of 87 drug related error were observed among them 45% were drug-drug interactions. 22% of interactions were of clinically significant need close attentions. Chronic kidney disease is now a day a prominent disease associated with hypertension and diabetic mellitus. Need proper assessment in order to prolong life and decrease hospitalization by providing rational therapy by avoiding all medication errors. Medication errors are avoidable events and it is the prime responsibility of pharmacist to detect it and handle it by discussing with health care professional like physician and nurses.

Keywords: Chronic renal failure; Medications errors; Roles of pharmacist; Inpatient; Tertiary hospital Peshawar

INTRODUCTION

Chronic kidney disease (CKD) is characterized by gradual loss of kidney function over a period of time. CKD is classified in to five major classes on the basis on decrease in renal function[1] Typically, CKD has no treatment. However, there are many strategies to reduce or control the sign and symptom, complication and to slow down aggravation. Diabetic is the most common cause of CKD in most of the developing countries including UK [2]. Along with diabetic hypertension is also most common cause of CKD[3]. The modification of diet in renal failure studies and researches indicate that control of hypertension is much more important for a chronic patient having Proteinuria level above 1gram per day[4].The prevalence of CKD is increasing globally[5]. During survey in 1999-2004 the ratio of CKD for adult >20years was 16% in United states [6] the ratio of hypertension and diabetic patients in Pakistan is going to increase day by day so as result the prevalence of CKD also increase

directly[7]. According to survey conducted in 2005 which stated that 180 million populations are prone to CKD including other concurrent disease like DM and HT which further increase the burden of CKD in rapidly urbanizing countries of south Asia like Pakistan as compared to country having low birth weight[8]. Prescribing medications is multidisciplinary process and it is one of the most common and highly risk area for physicians. [9] The most common medical error taking places in the hospitals are medication errors. A survey was conducted on medical error which shows that 44,000 to 98,000 patients expired as a result of medical errors in which 7,000 deaths occur as a result of medication errors which are too much high [10]. Medication error directly or indirectly increases cost and prolong the hospital stay of patients significantly [11]. Most often medication error arises during prescribing drugs, dispensing and administration of drugs by physician, pharmacist and nurse respectively[12]. Same like this in 2003 Barber and colleagues broadly classified medication errors in to three categories which include prescribing error, dispensing error and administering error .[13] But the most common and prevalent types of medications errors arise during treating patients are prescribing wrong drugs, prescribing drugs without indications, poly pharmacy which is the most common cause of drug PDDI, dispensing wrong drugs (look alike or sound alike medicine), or most often administering in a wrong way or wrong dilution [9]. It is quite important to keep implement clinical pharmacist in each ward in order to prevent all type of medication error by helping with all healthcare professionals. All previous studies concluded that prescribing to CKD patients need modification in the prescription because CKD populations are close to further nephrotoxicity[14]. The most common error while treating chronic kidney failure patient arises is antibiotic dose adjustment. Because antibiotic need close monitoring and dose adjustment in CRF patients based on e GFR[15]. Drug- drug interaction is also one of the major reason arise as a result of poly pharmacy which contribute to adverse effect little bit and lead to irrational therapy. The frequency of drug interaction depends on number of medicine prescribed, age of patients and the number of physician involved while treating patient. [16] For this reason pharmacist play a key role in preventing all these medication related errors like dose adjustment in CKD patients, dose calculation in paediatric population , compounding drugs for special case, preventing drugs- drugs interactions and therapeutic duplications, monitoring of narrow therapeutic drugs especially in CKD patients, avoiding poly pharmacy, preventing drugs with indication prescription and also playing a vital role in cost effectiveness of patients.

STUDY GOALS

The goal of this study was to document and then report medication error through systemic way in order to prove the importance of clinical pharmacist at ward level.

METHODOLOGY

The data was collected from 16th august 2015 to 19th January 2016 territory hospital of Peshawar kpk providing services of health care to most of the population of kpk. It was departmental project based study assigned by department of pharmacy Kohat University of science and technology.

STUDY COLLECTION AND DESIGN

For the collection of patient medication record a special profarma was design by the department of pharmacy. The profarma include patient demographics data, patients PR number, patient interview and admission date, chief complaint, biochemical test advice, diagnosis, prescribed medications (including date of prescription, therapy advice trade name, and their strength, frequency along with intervention by pharmacist and stop date and its reason), complaint about drug therapy, past medication record, any concurrent alignment, previous surgery record, response to present therapy, social history ,side effect and record of drug interaction etc.

All the data were collected from the nephrology ward by regular following up of patients who were admitted in the hospital. Medication records of 60 patients were included from 16 august to 19 January. The data were collected in order to analyze the drug related error which is arising due to many reasons.

Following data were collected for further analysis

- Patients demographic data
- Chief complaint
- Laboratory data report on regular base
- Diagnosis
- Treatment at hospital
- Past medication history
- Past surgical history
- Social history
- Adverse effect

Currents therapy which was provided in the hospital were analyze for following main drug related errors

- Uncontrolled condition
- Drug prescription without indications
- Improper drug selection
- Adverse related effects
- Drug interactions
- Non-compliance
- Drugs need dose adjustment in renal patients
- Therapeutic duplications
- Selection of inappropriate dosage foam
- Poly pharmacy
- Cost related problem

RESULT

Demographic consideration

Of all the 60 patients 35% were male and 65% were female as shown in the table No: 01 which show the increase prevalence of CKD in female as compared in male. 45% of affected pollution were uneducated while 25% & 16% of them were matriculate and collegiate respectively. Only 10% were got the degree of graduation and 6.6% were reaching to post-graduation. Age wise distribution of CKD were found to be more prevailing in aged population of having age range from 46-60 years the ratio of which was 55% whereas the lowest ratio were observed in younger population of having age distribution range from 18-34 years as shown in the table NO:01 below.

Co-morbid illnesses or concurrent disease

Among affected population the prevalence of hypertension among chronic renal patients were 53.33% while on the other side diabetic mellitus was observed in 20% of the population of CKD. 8.33 % people were detected for both diabetic and hypertension concurrently with CRF. Beside them 1.6%, 1.6% and 15% of the patients was reported for hepatitis-c, COPD, and UTI respectively along with kidney failure as shown in the table No: 01

Frequency of drug related problems

Among 60 hospitalized patients a total of 87 drugs related problem were identified. The drugs related errors were classified in to eight classes. The most common drug related problem which was detected after analysis was DDI (drug-drug interactions) the ratio of which was 45.97%. The frequency of adverse related errors was also high which was reported to 10.34%. Majority of them were avoidable. Prescribing drug without indication was also common. The ratio of which was 6.89%. Beside them the prevalence of other common drug related problem like untreated condition, non-compliance, drug needed dose adjustment, use of narrow therapeutic drugs without monitoring, poly pharmacy and cost related problem was 4.55%, 4.55%, 5.74%, 5.74%, 4.55%, 2.2% and 3.44% respectively. The practice of selecting inappropriate dosage form was negligible.

Potential drug interaction recorded were classified in to three categories on the basis of clinical significance which includes potentially significant, importance/moderately clinical significance and minor or low clinical significance. Overall 40 potential drug interactions were recorded of which 22% were clinically significant & 57% and 20% were important/clinically moderate and minor/low clinically significant respectively.

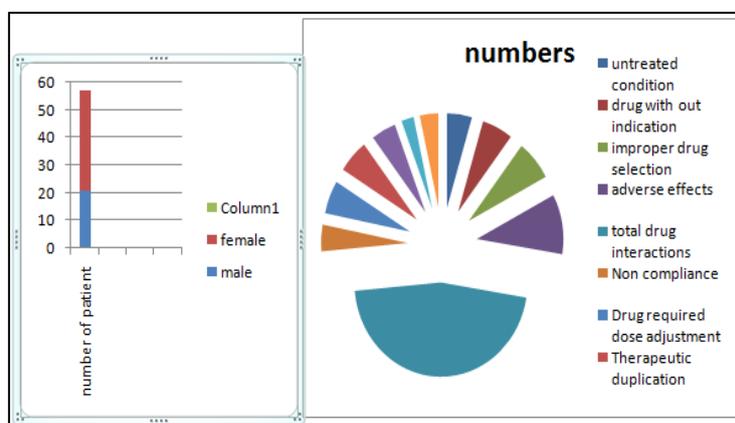


Figure 1: Diagrammatic Representation of (a) number of male and female ratio (b) types of medication errors

Table 1: Co-morbid illnesses or concurrent disease

Variables	N (%)
Gender	
Male	21 (35)
Female	39(65)
Age groups (years)	
18-30	3(5)
31-45	12(20)
46-60	33(55)
61-70	12(20)
Co-morbid illnesses or Concurrent disease	
Diabetics	18(20)
Hypertension	26(53.33)
Hepatitis –c	01(1.6)
COPD	01(1.6)
UTI	09(15)
Both HTN & DM	05(8.33)
Frequency of drug related problems	
Untreated condition	4(4.59)
Drug without indication	5(5.74)
Improper drug selection	6(6.89)
Adverse drug reaction	9(10.34)
Total drug interaction	40(45.97)
Non compliance	4(4.59)
Drug required dose adjustment	5(5.74)
Therapeutic duplication	5(5.74)
Inappropriate dosage form	0(0)
Use of narrow therapeutic drugs	4(4.59)
Polypharmacy	2(2.2)
Cost related problems	3(3.44)
Total	87
Prevalence of Potential drug drugs interactions (pDDI)	
Types of pDDI	
Highly clinically significance	
Important/serious/Moderately clinically significance	07(22.5)
Minor/ low clinical significance	22(57.5)
List of common DDI	
Minor/ low clinical significance	
Sucralphate and ciprofloxacin	07(20)
Omeprazole and carvedilol	1(2.5)
Sodium picosulphate and Itopride	1(2.5)
Furosemide and tamsulosin	1(2.5)
Folic acid and aspirin	1(2.5)
Dexametasone and aspirin	1(2.5)
Aspirin and furosemide	1(2.5)
Important/ serious/Moderately clinically significance	
Furosemide and alprazolam	1(2.5)
Alprazolam and tamsulosin	1(2.5)
Dexametasone and ciprofloxacin	1(2.5)
Dexametasone and moxifloxacin	2(5)
Albuterol and furosemide	2(5)
Ciprofloxacin and Sevelamer	2(5)
Cefotaxime and furosemide	2(5)
Furosemide and esomeprazole	2(5)
Cefexime and furosemide	2(5)
Cefotaxime and calcium gluconate	2(5)
Diphenhydramine and alprazolam	2(5)
Diphenhydramine and nalbuphine	2(5)
Alprazolam and diphenhydramine	1(2.5)
Hydrocortisone and prednisolone	1(2.5)
Loperamide and nifedipine	1(2.5)
Dexametasone and alprazolam	1(2.5)
Dexamethasone and enoxaparin	1(2.5)
Dexamethasone and ondansetron	1(2.5)
Highly clinically significance	
Nifedipine and amlodipine	1(2.5)
Epinephrine and azithromycin	1(2.5)
Epinephrine and furosemide	1(2.5)
Tramadol and dimenhydrinate	1(2.5)
Moxifloxacin and ondansetron	1(2.5)
Dobutamine and dopamine	1(2.5)

Most of them were repeated for more patients. All the histories collected were analyzed on a regular basis by comparing it with a standard guide line given in different resources like Laxi-comp, BNF-67, drug info sync online, Micromedex online, global RPH online, stock lay drug interaction handbook, medical drug interaction and indication etc for their rational use in order to increase patient better outcome.

DISCUSSION

Medication related error occurs commonly in all health care units. In this study prevalence medication related error with hospitalized patients were detected and reported. A total of 60 patient medication histories were studied. Important finding in this study was the medication error reported as a result of poor prescribing and to subject the importance of pharmacist in the clinical setup. In Pakistan the ratio of chronic kidney failure is increasing day by day. Hundred out of million cases have been recently reported of CKD [17]. This study includes 60 case histories of chronic kidney failure patients among them 65% were female and 35% were male which show high prevalence of ESRD in female. Previous studies also show increase prevalence of ESRD in female than male because female are more prone to diabetic [18]. Age of patients between 40-60 years was more prone to CKD which was 55% of all data. A study in 1985 by HIDA, M whose studies demonstrate people age in between 40-60 years are more affected by CKD [19]. The reason may be high due to risk of concurrent disease with CKD like diabetic and hypertension or some other age related changes. It was also concluded from the result that 55% of people having hypertension concurrently with CKD. On the other hand 20% of them were diabetic because high blood pressure and diabetic mellitus are the most common risk factor for deteriorating function of kidney [3, 20].

Total of 87 medication related error were reported by pharmacist in the nephrology ward where complete care was given mostly to acute and chronic kidney patients. The practice of detection and prevention of medication error is most common in North America [21]. A total of 60 prescriptions, resulting in 580 prescribed drugs in which 9 drugs per patient were prescribed. Medication error rate was 6.6 % (87 out of 580). The most common error found in this practice was prescribing medication having interactions as shown in the table NO: 05 & 06. The overall prevalence of drug-drug interaction was 45.97% among all medication error. Drug-drug interaction were classified in to 3 types on the basis of clinical significance either it may be highly significant, moderately significant or having low clinical significance [22]. In our study the ratio of important highly clinical significant/potentially severe, important/serious/moderate clinical significant and minor/low clinical significant were 20.68%, 22.98%, 60.25% respectively. Result of this study show that the prevalence of moderate and potentially severe type drug interaction was too much high which need to evaluate and highlighted in order to prevent in future. The reason behind these interactions was the increase number of prescribed medicine per patient. Previous studies also view the same result that as the number of drugs increase per patient the prevalence of drug interaction will be high [23-28], [26, 29]. The frequency of prescribed medication having moderate serious or clinically significant interaction was 57.5% (23 out of 40) while that of high clinical significant and low clinical significant were 22.3% and 20% of all respectively as shown in the table: 05 & 06.

Overall 34 type of drug interaction were detected out of 40 among which some of them were repeated. Clinically significant interaction includes co prescription of moxifloxacin and ondansetron because both of them contribute to prolong QT interval which may be fatal and lead to arrhythmias [30]. Likewise prescription of (amlodipine and nifedipine) calcium blocking agent at the same time to patient orally may lead to hypotension and also nifedipine increase the half-life of amlodipine by blocking metabolizing enzyme [31]. Sevelamer decrease the oral bioavailability of ciprofloxacin because of complex formation between quinolone and Sevelamer and calcium product when given orally at the same time so to avoid this interaction it is necessary to administered at different time [32].

The effect of carvedilol is increase by omeprazole because ppi mostly inhibit the enzyme responsible for the metabolizing of these drug at liver so need close monitoring which prescribing such type of drugs [33]. Administration of nifedipine with loperamide will decrease the level and effect of loperamide by inhibiting p-glycoprotein efflux transporter by nifedipine [34]. Therapeutic effect of ciprofloxacin is also decrease by co prescribing with Sucralphate [35, 36]. Close monitoring for sedative effect of tramadol and dimenhydrinate are necessary because both of them highly prone to sedation [37] administration of furosemide and epinephrine decrease potassium level in serum cause electrolyte imbalance lead to cardiac arrhythmias so need close monitoring [38].

Studies conducted since 1995 on drug related problem which increase cost on patient have more than double which is mostly occur as a result of prescribing drug without indication [39]. The ratio of prescribing drug without indication was 5.74% so it is necessary for health care organization to make rules and policy in order to prevent it. The ratio of improper drug selection was found to be 6.89% in this study. Drug given to patient without proper selection lead to medication error because if patient need therapy for medical problem and you prescribed wrong drug so it's called improper drug selection and it is most commonly occurring during selection chemotherapeutic agents. [40] it has been stated by American Society of Health-System Pharmacists that adverse

reaction is the six most common leading cause of death in hospitalized patients in united states. According to this analysis prevalence of adverse reaction was 10.34% which is same ratio as studies conducted previously in united states whose reported 5-20% ratio [41,42]. previously a lot of studies was conducted on the noncompliance problem which is a big issue for all health care professional that patient noncompliance with medication lead to non-effectiveness of therapy but it is mostly occur in outpatient.

As compared to outpatient the ratio of noncompliance in hospitalized patient was found to be negligible the ratio of which was 4.55%. beside these medication problem in hospitalized patients some other problem like therapeutic duplication, improper dosage form selection , poly pharmacy and cost related problem which lead to failure of therapy and most upon increase the length of hospitalization, increase extra cost on patient .

Medication related error occur everywhere at the health care unit but the rate of these error will be approximately 50 time less than that setting where clinical pharmacist play their role in ward setting actively. Because clinical pharmacist has unique knowledge regarding therapeutic and patient drug management at all levels. Pharmacist intervention in prescription, administration could prevent all medication related error by providing complete care with other healthcare unit (include nurse and physician) [43]. Multiple institute medication report identifies the importance of pharmacist in a healthcare unit by providing safe medication use for hospitalized patient. This study also realized that pharmacist-physician collaboration is much more important for patient safety [44,45].

CONCLUSION

Medications errors are avoidable events mostly occur in prescribing by physicians, dispensing by pharmacist, and administering by nurse. It is the prime responsibility of pharmacist to detect and prevent these medication related error with the cooperation of all healthcare professionals. It is necessary to make sure the presence of pharmacist at ward. Active role of clinical pharmacist is one of the best ways in order to reduce risk of being harmed by medication related errors. Drug-drug interaction were the most common medication error in overall, thus by study recommends strictly to implement policy for the prevention of drug-drug interactions.

REFERENCES

- [1] G Mortality. *Lancet*, **2015**, 385, 117-171.
- [2] Control, CfD and Prevention, National Chronic Kidney Disease Fact Sheet: general information and national estimates on chronic kidney disease in the United States, 2010. Atlanta, GA: US Department of Health and Human Services (HHS), CDC, **2010**.
- [3] GL Bakris; E Ritz. *J Clin Hyperten*, **2009**, 11(3), 144-147.
- [4] Control, CfD. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, **2011**. 201.
- [5] EAM Nahas; AK Bello. *Lancet*, **2005**, 365(9456), 331-340.
- [6] YJ Sheen; WH Sheu. *World J Diab*, **2014**, 5(6), 835-846.
- [7] YJ Sheen; WH Sheu. Name of journal: World Journal of Diabetes ESPS Manuscript NO: 12323 Columns: Review Risks of rapid decline renal function in patients with type 2 diabetes.
- [8] TH Jafar; BA Haaland; A Rahman; JA Razzak; M Bilger; M Naghavi; AH Mokdad; AA Hyder. *Lancet*, **2013**, 381(9885), 2281-2290.
- [9] K Khowaja; R Nizar; RJ Merchant; J Dias; I Bustamante-Gavino; A Malik. *Therap Clini Risk Manage*, **2008**, 4(4), 673-679.
- [10] IO Medicine. Preventing Medication Errors: Quality Chasm Series, National Academies Press Washington, DC, **2006**.
- [11] JT Davis. *Ann Thora Surg*, **1995**, 59(5), 1074-1078.
- [12] R Kaushal; DW Bates C Landrigan; KJ McKenna; MD Clapp; F Federico; DA Goldmann. *JAMA*, **2001**, 285(16), 2114-2120.

- [13] N Barber; M Rawlins; BD Franklin. *Qual Safety Health Care*, **2003**, 12(sup1), i29-i32.
- [14] A Corsonello; C Pedone; F Corica; C Mussi; P Carbonin; RA Incalzi. *Arch Inter Med*, **2005**, 165(7), 790-795.
- [15] A Farag; AX Garg; L Li; AK Jain. *Am J Kid Dis*, **2014**, 63(3), 422-428.
- [16] RM Seymour; PA Routledge. *Drugs Aging*, **1998**, 12(6), 485-494.
- [17] N ul Amin; RT Mahmood; MJ Asad; M Zafar; AM Raja. *J Cardiovas Dis*, **2014**, 2(2), 1-4.
- [18] RF Dyck; ND Osgood; TH Lin; A Gao; MR Stang. *Can J Diab*, **2010**, 34(4), 324-333.
- [19] M Hida; H Saito; T Wakabayashi; T Satoh. *Tokai J Exp Clin Med*, **1985**, 10(6), 581-588.
- [20] N Drey; P Roderick; M Mullee; M Rogerson. *Am J Kid Dis*, **2003**, 42(4), 677-684.
- [21] BJ Kopp; BL Erstad; ME Allen; AA Theodorou; G Priestley. *Crit Care Med*, **2006**, 34(2), 415-425.
- [22] RP Riechelmann; IF Tannock; L Wang; ED Saad; NA Taback; MK Krzyzanowska. *J Nat Cancer Inst*, **2007**, 99(8), 592-600.
- [23] M Pirmohamed; J Sally; M Shaun; G Chris; AK Scott; K Farrar; BK Park; AM Breckenridge. *BMJ*, **2004**, 329(7456), 15-19.
- [24] JH Gurwitz; TS Field; LR Harrold; J Rothschild; K Debellis; AC Seger; C Cadoret; LS Fish; L Garber; M Kelleher; DW Bates. *JAMA*, **2003**, 289(9), 1107-1116.
- [25] DJ Cullen; BJ Sweitzer; DW Bates; E Burdick; A Edmondson; LL Leape. *Crit Care Medi*, **1997**, 25(8), 1289-1297.
- [26] SS Egger; J Drewe; RG Schlienger. *Eur J Clin Pharmacol*, **2003**, 58(11), 773-778.
- [27] WC Lau ; LA Waskell; PB Watkins; CJ Neer; K Horowitz; AS Hopp; AR Tait; DG Carville; KE Guyer; ER Bates. Atorvastatin reduces the ability of clopidogrel to inhibit platelet aggregation a new drug–drug interaction. *Circulation*, **2003**, 107(1), 32-37.
- [28] K Johnell; I Klarin. *Drug Safety*, **2007**, 30(10), 911-918.
- [29] RM Goldberg; J Mabee; L Chan; S Wong. *Am J of Emerg Med*, **1996**, 14(5), 447-450.
- [30] MJ Armahizer; AL Seybert; PL Smithburger; SL Kane-Gill. *J Crit Care*, **2013**, 28(3), 243-249.
- [31] M Katoh; M Nakajima; N Shimada; H Yamazaki; T Yokoi. *Eur J Clin Pharmacol*, **2000**, 55(11-12), 843-852.
- [32] MB Kays; BR Overholser; BA Mueller; SM Moe; KM Sowinski. *Am J Kid Dis*, **2003**, 42(6), 1253-1259.
- [33] CYP2C9 CC and CA CYP2D6. *Am Fam Physician*, **2007**, 76, 391-396.
- [34] C Wandel; R Kim; M Wood; A Wood. *J Am Soc Anesthesiol*, **2002**, 96(4), 913-920.
- [35] JC Garrelts; PJ Godley; JD Peterie; EH Gerlach; CC Yakshe. *Antimicrob Agents Ch*, **1990**, 34(5), 931-933.
- [36] DE Nix; WA Watson; BSLHandy; RW Frost; DL Rescott; HR Goldstein. *J Human Pharmaco Drug Therap*. **1989**, 9(6), 377-380.
- [37] T Bidgood. *Managing Drug Toxicities & Drug Interactions: Clinical Pharmacology Case-Based Discussion*.
- [38] CB Bowling; B Pitt; MI Ahmed; IB Aban; PW Sanders; M Mujib; RC Campbell; TE Love; WS Aronow; RM Allman; GL Bakris; A Ahmed. *Circulation: Heart Failure*, **2010**, CIRCHEARTFAILURE. 109.899526.
- [39] FR Ernst; AJ Grizzle. Drug-related morbidity and mortality: updating the cost-of-illness model. *J Am Pharm Assoc-Washington*, **2001**. 41(2), 192-199.
- [40] SB Levy. *Sci Am*, **1998**, 278(3). 32-39.

[41] MC Lakshmanan; CO Hershey; D Breslau. *Arch Intern Med*, **1986**, 146(10), 1931-1934.

[42] HG Colt; AP Shapiro. *J Am Geriat Soc*, **1989**, 37(4), 323-326.

[43] PJ Kaboli; AB Hoth; BJ McClimon; JL Schnipper. *Arch Inter Med*, **2006**, 166(9), 955-964.

[44] LT Kohn. *Academic Health Centers:: Leading Change in the 21st Century*, National Academies Press, **2004**.

[45] LT Kohn; JM Corrigan; MS Donaldson. *To err is human*. Washington, DC: Institute of Medicine. National Academy Press, **2000**.