



## IMPACT OF MEDICAL RECONCILIATION IN TRANSITIONS OF CARE FOR PATIENTS WITH CARDIOVASCULAR DISEASES

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### ABSTRACT

Medical reconciliation is done to avoid medication discrepancies. It should be done at all transitions of care in which new medications are ordered or existing orders are rewritten. Cardiology patients have greater chances of getting medication discrepancies. The goal of this study is to bring out a rational prescribing pattern during transitions of care and to reduce medication errors, adverse drug events, drug interactions, treatment costs, drug related problems which lead to re-hospitalization. This was a prospective interventional study conducted in cardiology department of a tertiary care hospital with historical control. In control group, chart review was performed to identify drug

related problems (DRPs). In test group, best possible medication history (BPMH) was taken within 48 hours of admission and medical reconciliation was done to identify drug related problems. These drug related problems were classified according to Pharmaceutical Care Network Europe Foundation (PCNE) Version 6.2. The most commonly identified problems were untreated indication, non-allergic adverse drug event, unnecessary drug treatment and drug interactions which were caused by drug selection, inappropriate timing of administration and prescribing error. Factors associated with occurrence of DRPs include middle age, administering more than 10 drugs and in-hospital stay. Some of these DRPs were brought to the notice of the prescribers and eventually solved. Thus, the involvement of clinical pharmacist in conducting medical reconciliation will help ameliorate drug related discrepancies in transitions of care.

**KEYWORDS:** Medical reconciliation, Drug related problems, Cardiology, PCNE V6.2.

## MATERIALS AND METHODS

This is a prospective interventional study conducted in Department of Cardiology, PSG Hospitals. It is a multi-speciality tertiary care teaching hospital having more than 900 beds. The study was approved by Institutional Ethics Committee (IHEC, PSGIMS&R). The proposal number is 17/067 dated on 23/02/2017. The study was conducted for a period of 6 months in the year 2017.

As per Raosoft software, the sample size was estimated to be 100 per group (200 in total) considering the fact that there would be 5 admissions per day in the Department of Cardiology, PSGIMS&R. The margin of error accepted, confidence interval, and response distribution were calculated to be 10%, 95% and 50% respectively.

Out of 200 patients, 98 patients from control group and 96 patients from test group met inclusion and exclusion criteria making a sum of 194. The statistical test used was Odds Ratio to find the risk of having DRPs in control when compared to test after medical reconciliation and Pearson's Chi-square test for testing the significance (95% CI, 2 tailed).

The inclusion criteria for this study were patient willing to give consent, patients above 18 years of age, men and women with at least 3 prescribed drugs, cardiology patients, pregnancy and lactation. The exclusion criteria for this study were psychiatric disturbances, death and discharge within 24 hours.

The study contains one control group and a test group. The control group was taken from the medical record department where medical reconciliation was not performed (historical control). The test group was taken from inpatients of cardiology department where medical reconciliation was performed. Patients voluntarily gave informed consent to participate in this study. In control group done retrospectively, case files were taken from the medical records department of PSG hospitals. Medication chart review was performed followed by identification and classification of drug related problems. In test group, the steps for reconciliation at admission included taking the best possible medication history (BPMH) within 48 hours. *Verification* by comparing the BPMH with admission medication order; *Clarification* by checking the appropriateness of dosages and drugs; *Reconciliation* by evaluating the newly initiated drugs and finally identifying and classifying DRPs.

At discharge, *Verification* was performed by comparing BPMH, admission medication order and new medicines on discharge; *Clarification* by checking appropriateness of dosages and drugs; *Reconciliation* by resolving and documenting discrepancies followed by identification and classification of DRPs.

The tools used were Pharmaceutical Care Network Europe Foundation (PCNE) Classification: Version 6.2 for classification of drug related problems<sup>[24]</sup>, Micromedex Drug Interactions; Truven Health Analytics 2017 for checking drug interactions, American Heart Association Guidelines for Cardiovascular Diseases to check the rationale of drug therapy, Microsoft Excel 2010 spreadsheets, SPSS Version 16.0 were used to analyse the data statistically.

## RESULTS AND DISCUSSION

A total of 200 subjects were classified into 4 different age groups; 18 - 39 years (11%), 40 - 59 years (48.5%), 60 - 79 years (39.5%), 80 - 99 years (1%), of which majority were under the 40-59 years (48.5%) in comparison to a study where the prevalence of CVD increases with age and is very high in 41-60 years.<sup>[38,50]</sup> This might be due to the sedentary lifestyle of youngsters which later become a risk factor for CVD in middle aged. We need to be more aggressive at fostering healthy lifestyles in young people. In this study the predominant gender was male (66.5%) than female (33.5%) in contrast to the above study<sup>[50]</sup> by *Bani T Aeri et al* where females kept in pace with males. This marks the stressful events such as social isolation, excessive alcohol consumption and smoking. High levels of estrogen protect women from cardiovascular diseases until their menopause. Most patients (54.31%) came under normal BMI (18-25kg/m<sup>2</sup>) category followed by overweight (25%), obese (13.79%) and underweight (6.89%). According to Kaur P et al, BMI  $\geq 23$  kg/m<sup>2</sup> is considered a risk factor for CVD.<sup>[51]</sup> The occurrence of CVD might be due to the existing co-morbidities, family history in these patients and not because of weight.

About 45% had diabetes, 36.5% with hypertension, followed by dyslipidemia (14%), respiratory diseases (4%) and heart diseases (35%) which is similar to a study by *wantsenghsu et al.*<sup>[5,7]</sup> Multiple co morbidities account for most ADRs in elderly as per *Hasniza et al.*<sup>[21]</sup> Cardiology patients had a high mean number of co-morbid conditions as per *Unroe et al.*<sup>[1]</sup> Connection between diabetes and heart disease starts with high blood sugar levels. 8.5% of the patients had a family history of diabetes mellitus and heart disease followed by hypertension (3.5%). People with family history of heart diseases are more prone to develop

CVD. 29% of the patients were smoker followed by alcoholic (16.5%) and tobacco users (3%). According to *Javeedh et al*, these are risk factors that influences the levels of blood clotting factors such as fibrinogens.<sup>[38]</sup> Nicotine raises blood pressure and CO reduces the amount of oxygen that blood can carry.

Medication history interview was possible only in the test group (100 patients). So, OTC drug use, herbal product use, drug and food allergy information was obtained from these patients. 28% of the test group used OTC drugs (mostly NSAIDs) in whom some took vitamin supplements which was reported to prescribers unlike study by *Unroe et al* where vitamins use were not reported as a discrepant.<sup>[1]</sup> 15% of the test group used herbal medicines prior to admission and according to Andrew et al DRPs related to more than two drugs involved examples such as St John's Wort interacting with a number of medications or the combination of NSAID, ACEI and diuretic combinations potentially affecting renal function. 9% were allergic to some drugs like penicillin and certain foods. These did not cause any DRPs as the health care team were aware of allergies and treated accordingly.

Among 194 patients (98 in control group and 96 in test group) included in the study, 79 patients (38 in control group and 41 in test group) had drug related problems (DRPs) and  $P > 0.05$  showed insignificance. (Table 1) Numerous studies have concluded that cardiovascular medications are the most common drug class associated with the occurrence of DRPs.<sup>[21]</sup>

**Table 1: Number of patients having drug related problems.**

Population	NO. OF Patients Having DRPs (%)	NO. OF Patients NOT Having DRPs (%)	'P' Value
CONTROL (N=98)*	38 (48.10)	60 (52.63)	0.536
TEST (N=96)\$		41 (51.89)	54 (47.36)

*No of patients excluded in control=2 patients\**

*No of patients excluded in test=4patients \$*

*control does not have any risk*

Table 2 shows that the overall percentage in this study for distribution of problems as per PCNE in control and test which include treatment effectiveness (34.04%, 36.53%), adverse reactions (2.12%, 7.69%), treatment costs (6.38%,9.61%), others (57.44%,46.15%) with a  $P > 0.05$ . The result of adverse reactions are less in control and more in test when compared to a study done by *Abdul Khalil et al* where the occurrence of ADR was 6.25%.<sup>[6]</sup> Highest

occurrence of DRPs is in other problems as per PCNE because drug interactions are classified under this as there is no separate category in V6.2. It will be better to include a separate category for drug interactions as it was in V5.01. The occurrence of DRPs is high in other problems followed by treatment effectiveness, treatment costs and adverse reactions.

The overall percentage for distribution of causes as per PCNE in control and test which include drug selection (40.42%,44.23%) with  $P>0.05$ , dose selection (2.12%, 3.84%) with  $P>0.05$ , drug use process (44.68%, 23.07%) with a significant  $P=0.023^*$ , logistics (10.63%,3.84%) with  $P>0.05$ , patient (0%,11.53%) with a significant  $P=0.016^*$ , other (2.12%, 13.46%) with a significant  $P=0.039^*$  as in Table 2. The significant P value proves the need for medical reconciliation. The most common cause is drug selection because of untreated indication followed by drug use process, other causes, patient as cause and logistics, dose selection. The assignment of causes to each DRP was based on our own judgement or from information obtained from the medical records, which lead to difficulties in assessing the causes of DRPs, as some possible causes of DRPs may not be retrievable from medical records for the control group.

Categorisation of interventions in control and test includes no intervention (23.40%,17.30%) and intervention (76.59%,82.69%). Examples for problems with no intervention includes NAC not given in CKD during discharge, OROFER XT (ferrous ascorbate + folic acid) prescribed instead of LIVOGEN (ferrous fumarate + folic acid) in discharge, route of administration of a syrup was written as IM, documentation error involving time of administration of drug, pantoprazole was not administered yet documented, untreated anemia, BPH. These discrepancies were not intervened as they occurred in discharge medications. This is due to untimely identification of DRPs.

The overall percentage for distribution of interventions as per PCNE in control and test as shown in table 2 includes; at prescriber level (76.59%,65.38%) with a significant  $P=0.004^{**}$ . At patient/carer level (0%,13.46%) with a significant  $P=0.011^*$ . At drug level (0%,1.92%) with  $P>0.05$ . Other intervention/activity (0%,1.92%) with  $P>0.05$ . More number of interventions is found in prescriber level followed by patient/ carer level and drug level. The significant P value shows the effect of medical reconciliation. Another study showed that intervention at prescriber level attributed to 40.37% and interventions at patient/ carer level attributed to 6.83% which is less compared to our study and interventions at drug level attributed to 50.93% and it is very high compared to our study.<sup>[11]</sup>

Categorisation of outcomes in control and test include not known (21.27%, 19.23%) and known (78.72%, 80.76%) with  $P > 0.05$  which in comparison to a study show not known (6.83%) and known (93.16%).<sup>[11]</sup> The outcome of interventions that are not known for discrepancies such as unavailable dose of STARPRESS XL 150mg and that which occurred in retrospective group like untreated anemia, CKD, BPH. This necessitates medical reconciliation in hospital stay.

The overall percentage of outcome of intervention as per PCNE in control and test include solved (0%, 17.30%) with significant  $P = 0.003^{**}$ , partially solved (0%, 36.5%) with significant  $P = 0.000^{***}$  and not solved (78.72%, 26.9%) with significant  $P = 0.000^{***}$ . The outcome of intervention of DRPs was (partially) solved by informing the prescriber, stopping a drug and through patient education. This shows the need of medical reconciliation in a hospital. The significant P value shows that outcome of interventions is found only in test as the control group was taken retrospectively.

Distribution of problems in treatment effectiveness as per PCNE in control and test which includes effect of drug treatment not optimal (2.12%, 0%)  $OR = 0.902$  where control does not have any risk. In our study, ACEI / ARBs were not prescribed for a heart failure patient with reduced ejection fraction. The addition of ACEI/ARBs significantly reduces mortality and hospitalisations for heart failure in patients with CHF and low ejection fractions. So, re-hospitalisations can be reduced by performing medical reconciliation.

Untreated indication (31.91%, 36.53%)  $OR = 1.228$  in which control has a risk than test with  $P > 0.05$ . In comparison to a study, we found that untreated indication was only 3.77%.<sup>[38]</sup> In our study, the untreated indications were anemia, dyslipidemia, CKD, vertigo, liver cirrhosis, HTN, BPH, severe PAH, OA, hypothyroidism which is similar to a study done by *Javeedh et al* where anemia, cough, dyslipidemia, hypokalemia were untreated.<sup>[38]</sup> This problem might have occurred as these co-morbid conditions got unnoticed because of the severity of the condition for which the patient got admitted. So, medical reconciliation by clinical pharmacists are mandatory to reduce these discrepancies as they see that every indication is treated. There are no problems in sub-domains like no effect of drug therapy/treatment failure and wrong effect of drug treatment.



**Table. 2: Distribution of drug related problems as per PCNE V6.2 into primary domain.**

Code	Primary Domain	Control (%)	Test (%)	P Value
<b>PROBLEMS</b>				
<b>P1</b>	Treatment effectiveness	16 (34.04)	19 (36.53)	<b>0.795</b>
<b>P2</b>	Adverse reactions	1 (2.12)	4 (7.69)	<b>0.207</b>
<b>P3</b>	Treatment costs	3 (6.38)	5 (9.61)	<b>0.556</b>
<b>P4</b>	Others	27 (57.44)	24 (46.15)	<b>0.262</b>
<b>CAUSES</b>				
<b>C1</b>	Drug selection	19 (40.42)	23 (44.23)	<b>0.702</b>
<b>C3</b>	Dose selection	1 (2.12)	2 (3.84)	<b>0.618</b>
<b>C5</b>	Drug use process	21 (44.68)	12 (23.07)	<b>0.023*</b>
<b>C6</b>	Logistics	5 (10.63)	2 (3.84)	<b>0.188</b>
<b>C7</b>	Patient	0 (0)	6 (11.53)	<b>0.016*</b>
<b>C8</b>	Other	1 (2.12)	7 (13.46)	<b>0.039*</b>
<b>Interventions</b>				
<b>I0</b>	No intervention	11 (23.40)	9 (17.30)	<b>0.451</b>
<b>I1</b>	At prescriber level	36 (76.59)	34 (65.38)	<b>0.004**</b>
<b>I2</b>	At patient/carer level	0 (0)	7 (13.46)	<b>0.011**</b>
<b>I3</b>	At drug level	0 (0)	1 (1.92)	<b>0.357</b>
<b>I4</b>	Other intervention/activity	0 (0)	1 (1.92)	<b>0.357</b>
<b>Outcomes</b>				
<b>O0</b>	Not known	10 (21.27)	10 (19.23)	<b>0.800</b>
<b>O1</b>	Solved	0 (0)	9 (17.30)	<b>0.003**</b>
<b>O2</b>	Partially solved	0 (0)	19 (36.5)	<b>0.000***</b>
<b>O3</b>	Not solved	37 (78.72)	14 (26.9)	<b>0.000***</b>

Table 3 shows that distribution of problems related to adverse reactions as per PCNE in control and test includes non-allergic adverse drug event (0%,5.76%) such as nitroglycerin induced headache with OR =1.083 where control has a risk than test with insignificant  $P > 0.05$ . This can be resolved with a dose of acetaminophen if the headache persists for half an hour. Allergic adverse drug event (0%, 1.92%) such as ramipril induced pedal edema with OR =1.020 where control has a risk than test and  $P > 0.05$ . This ADE was found and consequently ACEI was replaced with ARBs. These ADEs are patient specific and can be corrected only when it occurs. Since the results show a risk in control, medical reconciliation is essential. This is similar to a study where non allergic ADE is predominant than allergic ADE but none were found for toxic ADE.<sup>[11]</sup> Toxic adverse drug event (2.12%,0%) might have occurred when cefixime was used in CKD with OR=0.979 where control does not have any risk than test with  $P > 0.05$  is insignificant. This is due to different pharmacokinetics in CKD patients. In this study, ADRs are less represented because ADRs are traditionally more investigated than other DRPs.

Distribution of problems related to treatment costs as per PCNE in control and test includes drug treatment more costly than necessary (0%, 3.84%)OR =1.040 where control has a risk than test and unnecessary drug treatment (6.38%,5.76%)OR =0.898 where control does not have any risk with insignificant  $P>0.05$ . This economical issue is due to use of expensive brands. For example, in our study OROFER XT (ferrous ascorbate + folic acid) was used in place of LIVOGEN (ferrous fumarate+ folic acid) which is ten times more costly. OROFER XT can be used if the patient has anemia with gastric problems. Ascorbic acid improves the absorption of iron from the stomach. These results are similar to a study done by *Akram Ahmed et al* in terms of treatment costs (20.40%).<sup>[11]</sup> Treatment costs can also be reduced by medical reconciliation.

Distribution of other problems as per PCNE in control and test includes patient dissatisfied with therapy despite optimal clinical and economic treatment outcomes (0%,1.92%)with OR =1.020 where control has a risk than test with insignificant  $P>0.05$ . In our study, a patient denied the use of SEQUEDRA inhaler (indacaterol/glycopyrronium) as it was uncomfortable. This might result in breathing difficulties. These situations can be avoided by educating the patients through medical reconciliation. Unclear problem/complaint, further clarification necessary(57.44%,44.23%)OR =0.587 where control does not have any risk with  $P>0.05$ . This is similar to study where other problems constitute to 15.64%.<sup>[11]</sup> In our study, polypharmacy, prescribing errors and mostly drug interactions were classified under other problems.

Distribution of causes in drug selection as per PCNE in control and test includes inappropriate drug (2.12%, 4.34%) such as use of KETOADD (alpha keto analogue with essential aminoacids) in gout patient with OR=0.902 where control does not have any risk with  $P >0.05$ . The reason we could assume for this discrepancy is lack of time due to patient burden. Inappropriate duplication of therapeutic group/active ingredient (2.12%,4.34%) such as concurrent use of DIZITAC (cinnarizine) and BVERT (betahistine) for dizziness with OR=0.902 where control does not have any risk with  $P >0.05$ . Inappropriate drug selection can lead to unnecessary treatment cost which in turn increases patient's economic burden. Indication for drug treatment not noticed (29.78%,26.92%)such as iron supplements not prescribed for anemia, betahistine not given for dizziness and statins not prescribed for dyslipidemia with OR=0.868 where control does not have any risk with  $P >0.05$ . These discrepancies occurred as these conditions were overlooked. Too many drugs prescribed for



indication (2.12%,13.04%) such as use of PPI and H2 blockers with OR=2.816 where control has a risk than test with  $P > 0.05$ . When used together, the extensive acid suppression therapy may decrease the absorption of certain nutrients (vitamin B12, iron and calcium), which are dependent upon an acidic environment to be absorbed in the stomach. Combination therapy may also increase the risk of GI infections. This DRP might have occurred due to confusions among different healthcare systems. More cost-effective drug available (0%,8.69%) such as LIVOGEN (ferrous fumarate + folic acid) in place of OROFER XT (ferrous ascorbate + folic acid) with OR=1.040 where control has a risk than test with  $P > 0.05$ . This can be solved by assessing the economic background of the individual patient and prescribing the drugs accordingly. Synergistic/preventive drug required and not given (4.25%,8.69%) like NAC in CKD patients with OR=0.900 where control does not have any risk with  $P > 0.05$ . A study shows, the second documented DRP after potential drug-drug interaction (PDDI) was drug selection(33.75%) comprised of cost effective alternative(17.5%), inappropriate drug selection(8.75%), too many drugs for indication (5%) and no indication for drugs(2.5%) which is less compared to our study.<sup>[6]</sup>

Distribution of causes in dose selection as per PCNE in control and test includes drug dose too high (0%,1.92%) like giving cetirizine twice a day with OR=1.020 where control has a risk than test with  $P > 0.05$ . In geriatric patients, maximum dose of cetirizine is 10mg per day. So, high dose of cetirizine will enhance sedation. This type of discrepancy can be avoided by medical reconciliation. Dosage regimen too frequent (2.12%,1.92%) like Inj.Pan given 40mg twice a day with OR=0.902 where control does not have any risk with  $P > 0.05$ . Inj.Pan should be given 40mg once daily even in GERD. Twice a day regimen might lead to improper absorption of nutrients as discussed above. These causes show the overutilization of gastro protective agents. This can be reduced by putting more efforts into medication review whenever possible to reduce the risk of DRPs. A study shows that 42.2% of the causes are attributed to dose selection which is very high compared to our study.<sup>[11]</sup>

Distribution of causes in drug use process as per PCNE in control and test includes inappropriate timing of administration and for dosing intervals (51.06%,23.07%) in our study is the co-administration of pantoprazole and levothyroxine; aspirin and spironolactone with OR=0.371 where control does not have any risk with significant  $P=0.023^*$ . Concomitant use of levothyroxine and a proton pump inhibitor may cause significant increase in TSH levels. Proton pump inhibitors may lower stomach acid, decrease levothyroxine absorption, and

affect intra gastric pH. Administer levothyroxine four hours before/ after drugs that are known to decrease absorption. Concurrent use of NSAIDs and diuretics may result in reduced diuretic effectiveness, hyperkalemia, or possible nephrotoxicity. This cause has led to drug-drug interactions (DDIs) which was established based on standard references. This can be minimised by frequent monitoring of adverse events secondary to DDIs. This emphasizes the effect of medical reconciliation. A study by *Hasniza zamanhuri et al* shows an occurrence of drug use process (9.5%) which is less compared to our study.<sup>[21]</sup>

Distribution of causes in logistics as per PCNE in control and test includes prescribing error (10.63%, 3.84%) like spelling error; RCIN as REON, with OR=0.336 control does not have any risk where  $P > 0.05$ . This is due to illegible handwriting, patient load and time constraint. The errors found in this study are surprisingly very less in comparison to studies that show logistics (11.18%) which is high compared to our study.<sup>[11]</sup> These errors can be avoided through medical reconciliation.

Distribution of causes in patient as per PCNE in control and test includes patient forgets to use/take drug (0%, 1.92%) eg., an ulcer patient did not take esomeprazole on the day of discharge, with OR=1.020 where control has a risk than test with  $P > 0.05$ . This may lead to irritation in the stomach. Patient uses unnecessary drug (0%, 9.61%) like NSAIDs as OTC and cough syrups, with OR=1.020 where control has a risk than test with  $P > 0.05$ . NSAIDs use in CVD can lead to bleeding risk. This occurred due to lack of knowledge of the patient about the risks associated with the use of OTC. This emphasizes that a community pharmacist should not dispense drugs without prescription. Additionally, a clinical pharmacist can check a patient's drug use habits and thereby prevent these discrepancies. In comparison to a study where patient as cause has 2.48% which is less compared to test group of our study.<sup>[11]</sup>

Distribution of other causes as per PCNE in control and test includes other cause (2.12%, 11.53%) such as inability of the patient to buy/use a drug, with OR=6.000 where control has a risk than test with  $P > 0.05$ . This is because some patients are unaware of the severity of the disease condition. No obvious cause (0%, 1.92%) for the concurrent use of KCl and spironolactone, with OR=1.020 where control has a risk than test where  $P > 0.05$ . Concurrent use of potassium and spironolactone may result in hyperkalemia by decreasing renal clearance. This is an intentional discrepancy for increasing the levels of potassium in patients with low  $K^+$  levels. These combinations are used depending on patient requirement in par

with prescription policies. A study show that 1.43% of other causes which is less compared to our study.<sup>[9]</sup>

Distribution of interventions at prescriber level as per PCNE in control and test includes prescriber informed only (25%,18.60%) for discrepancies like untreated anemia, PAH in discharge, polypharmacy, with OR=0.980 where control does not have any risk with  $P>0.05$ . Prescriber asked for information (55.55%,27.90%) for DDI of aspirin and spironolactone, with OR=0.489 where control does not have any risk with  $P>0.05$ . Intervention proposed, approved by prescriber (19.44%,18.60%) like DDI of pantoprazole and levothyroxine. In this the absorption of levothyroxine is reduced when pantoprazole is co-administered as it makes the stomach alkaline. This can be avoided by different time of administration, with OR=1.523 where control has a risk than test with  $P>0.05$ . Intervention proposed, not approved by prescriber (0%,2.32%) in case of spelling error, with OR=1.020 where control has a risk than test with  $P>0.05$ . This did not cause any harm to the patient as the generic provided was correct. Intervention proposed, outcome unknown (0%,11.62%) for discrepancies that occurred during discharge, with OR=1.020 where control has a risk than test with  $P >0.05$  in comparison to study by *Abdul Khalil* showed that 18.75% of the interventions made were approved by the prescriber which is less in comparison to our study.<sup>[6]</sup> In our study, more number of interventions come under prescriber asked for information and least in intervention proposed, not approved by prescriber. This suggests that medical reconciliation can effectively identify and prevent clinically significant DRPs.

Distribution of interventions at patient/carer level as per PCNE in control and test includes patient counselling (0%,4.65%) for OTC drug use, with OR=1.040 where control has a risk than test with  $P>0.05$ . Patient referred to prescriber (0%,4.65%) for OTC drug use, with OR=1.040 where control has a risk than test where  $P>0.05$ . Spoken to family member/caregiver (0%,6.97%) as the patient was unwilling to use inhalers, with OR=1.061 where control has a risk than test with  $P>0.05$ . This discrepancy is due to lack of knowledge and difficulty in using inhalers. It can be minimised by proper demonstration by clinical pharmacist.

Distribution of interventions at drug level as per PCNE in control and test includes drug stopped (0%,2.32%) in case of polypharmacy, with OR=1.020 where control has a risk than test with  $P >0.05$ . This has avoided an occurrence of DRP which explains the effect of medical reconciliation.

Distribution of other interventions as per PCNE in control and test includes side effect reported to authorities (0%,2.32%) like nitroglycerin induced headache, with OR=1.020 where control has a risk than test with  $P>0.05$ . In comparison to another study where other interventions attributes to 1.86% which is less compared to our study.<sup>[11]</sup> The inconvenience related to the use of drug has been rectified through medical reconciliation.

Distribution of outcome of intervention in not solved category as per PCNE in control and test include problem not solved, lack of cooperation of patient (0%,7.14%) for the use of NSAIDs as OTC, with OR=1.020 where control has a risk than test where  $P>0.05$ . The patient refused to accept his use to the prescriber as he was afraid of prolongation of hospital stay. Problem not solved, lack of cooperation of prescriber (8.10%,7.14%) in accepting certain DRPs due to unmet communication, with OR=0.288 where control does not have any risk where  $P>0.05$ . Problem not solved, intervention not effective (0%,14.28%) for certain DRPs like inappropriate duplication of drugs (diltiazem and diltiazem SR), with OR=1.040 where control has a risk than test where  $P>0.05$ . No need/possibility to solve problem (91.89%, 71.42%) OR=0.091 where control does not have any risk with  $P>0.05$ . These conditions occur in retrospective group and in prospective group with untimely intervention. For eg., amlodipine can be replaced by cilnidipine in CKD patients as vasodilatory effects like pedel edema is not found in the later. 3

**Table. 3: Distribution of drug related problems as per PCNE V6.2 into secondary domain.**

CODE	SECONDARY DOMAIN	CONTR OL (%)	TEST (%)	ODD'S RATIO	P VALUE
<b>PROBLEMS</b>					
<b>P1.2</b>	Effect of drug treatment not optimal	1 (2.12)	0 (0)	0.902	0.942
<b>P1.4</b>	Untreated indication	15 (31.91)	19 (36.53)	1.228	0.629
<b>P2.1</b>	Adverse drug event (non - allergic)	0 (0)	3 (5.76)	1.083	0.052
<b>P2.2</b>	Adverse drug event (allergic)	0 (0)	1 (1.92)	1.020	0.339
<b>P2.3</b>	Toxic Adverse drug event	1 (2.12)	0 (0)	0.979	0.290
<b>P3.1</b>	Drug treatment more costly than necessary	0 (0)	2 (3.84)	1.040	0.174
<b>P3.2</b>	Unnecessary drug	3 (6.38)	3 (5.76)	0.898	0.898

	treatment				
<b>P4.1</b>	Patient dissatisfied with therapy despite optimal clinical and economic treatment outcomes	0 (0)	1 (1.92)	1.020	0.339
<b>P4.2</b>	Unclear problem/complaint. Further clarification necessary	27 (57.44)	23 (44.23)	0.587	0.189
<b>CAUSES</b>					
<b>C1.1</b>	Inappropriate drug (incl. contra indicated)	1 (2.12)	1 (4.34)	0.902	0.942
<b>C1.4</b>	Inappropriate duplication of therapeutic group or active ingredient	1 (2.12)	1 (4.34)	0.902	0.942
<b>C1.5</b>	Indication for drug treatment not noticed	14 (29.78)	14 (26.92)	0.868	.752
<b>C1.6</b>	Too many drugs prescribed for indication	1 (2.12)	3 (13.04)	2.816	0.358
<b>C1.7</b>	More cost effective drug available	0 (0)	2 (8.69)	1.040	0.174
<b>C1.8</b>	Synergistic/preventive drug required and not given	2 (4.25)	2 (8.69)	0.900	0.918
<b>C3.2</b>	Drug dose too high	0 (0)	1 (1.92)	1.020	0.339
<b>C3.4</b>	Dosage regimen too frequent	1 (2.12)	1 (1.92)	0.902	0.942
<b>C5.1</b>	Inappropriate timing of administration and/or dosing intervals	21 (51.06)	12 (23.07)	0.371	0.023*
<b>C6.2</b>	Prescribing error(necessary information missing)	5 (10.63)	2 (3.84)	0.336	0.188
<b>C7.1</b>	Patient forgets to use/take drug	0 (0)	1 (1.92)	1.020	0.339
<b>C7.2</b>	Patient uses unnecessary drug	0 (0)	5 (9.61)	1.020	0.339
<b>C8.1</b>	Other cause: specify	1 (2.12)	6 (11.53)	6.000	0.068
<b>C8.2</b>	No obvious cause	0 (0)	1 (1.92)	1.020	0.339
<b>INTERVENTIONS</b>					
<b>I1.1</b>	Prescriber informed only	9 (25)	8 (18.60)	0.980	0.970
<b>I1.2</b>	Prescriber asked for	20	12 (27.90)	0.489	0.107

	information	(55.55)			
<b>I1.3</b>	Intervention proposed, approved by prescriber	7 (19.44)	8 (18.60)	1.523	0.443
<b>I1.4</b>	Intervention proposed, not approved by prescriber	0 (0)	1 (2.32)	1.020	0.339
<b>I1.5</b>	Intervention proposed, outcome unknown	0 (0)	5 (11.62)	1.020	0.339
<b>I2.1</b>	Patient (medication counselling)	0 (0)	2 (4.65)	1.040	0.174
<b>I2.3</b>	Patient referred to prescriber	0 (0)	2 (4.65)	1.040	0.174
<b>I2.4</b>	Spoken to family member/care giver	0 (0)	3 (6.97)	1.061	0.094
<b>I3.5</b>	Drug stopped	0 (0)	1 (2.32)	1.020	0.339
<b>I4.2</b>	Side effect reported to authorities	0 (0)	1 (2.32)	1.020	0.339
<b>OUTCOMES</b>					
<b>O3.1</b>	problem not solved, lack of cooperation of patient	0 (0)	1 (7.14)	1.020	0.339
<b>O3.2</b>	problem not solved, lack of cooperation of prescriber	3 (8.10)	1 (7.14)	0.288	0.260
<b>O3.3</b>	problem not solved, intervention not effective	0 (0)	2 (14.28)	1.040	0.174
<b>O3.4</b>	no need or possibility to solve problem	34 (91.89)	10 (71.42)	0.091	0.000***

Frequency of DRPs per patient in control and test includes 1 DRP (32.65%,32.29%);2 DRP (6.12%,6.25%);3DRP (1.02%,0%);4DRP (1.02%,1.04%). A study done by *Gabriella et al* describes on frequency of discrepancies in patients.<sup>[17]</sup> Most patients have 1 DRP that might be due to contentment of the investigators.

Distribution of DRPs in transitions of care in control and test includes admission (0%,5.76%);in-hospital (46.80%,53.84%) OR=1.326 where control has a risk than test; discharge (12.76%,13.46%) OR=1.063 where control has a risk than test; both in-hospital and discharge (40.42%,26.92%) OR=0.543 where control does not have any risk with  $P>0.05$ . Most discrepancies were found in hospital stay and discharge as we were able to follow the patients at the right time. Medical reconciliation at admission demands a detailed BPMH which was taken as effective as possible.



Types of DRPs in control and test include intentional (5.76%,2.17%) and unintentional (94.23%,97.82%). A study showed that 17.7% of discrepancies were unintentional.<sup>[17]</sup> Most DRPs were unintentional due to omission of drugs rather than commission. The only intentional discrepancy was the concurrent use of Syp.KCl and spironolactone.

Among 194 patients followed during the study period, a total of 99 DRPs were found in 79 patients. Out of 79 patients, 62.02% were found in males and 37.97% in females. This result is similar to a study carried out by *Javeedh shareef et al* which showed male predominance over females. This might be due to increased medication use because of their multiple comorbid conditions and also possibility of various risk factors like smoking, alcoholism and a sedentary lifestyle etc. compared to female population.<sup>[38]</sup>

The incidence of DRPs was high in the age group of 40-59yrs in both control (50%) and test (68.29%) followed by 60-79yrs in both control (44.70%) and test (26.82%) similar to a study where it was 55.35% in patients aged between 41-60yrs. This indicate that special attention should be given in such group of patients were regular review of drug therapy might help potentially to decrease DRPs.<sup>[38]</sup>

Among the number of drugs, patients receiving more than 10 drugs were found to have more DRPs in both control (73.60%) and test (56.09%) which is similar to a study where patients receiving more than 6-10 drugs have more DRPs (52.30%).<sup>[38]</sup>

The limitations of this study were that there was no gold standard for obtaining BPMH. Also, it was difficult to intervene in timely manner when the discrepancy occurred in discharge medications. As we were not able to attend ward rounds, it was difficult to identify, intervene and solve problems. Unreliability and missing information in the medical records for chart review in retrospective group was also found. This was performed in one hospital ward in a single hospital with a limited number of patients. PCNE V 6.2 does not have a category for drug interactions. So, all drug interactions were classified under unclear problems. Only one cause, intervention and outcome were assigned for a problem as per PCNE version 6.2.

## CONCLUSION

Drug related problems were found in hospitalized patients. This was alleviated through medical reconciliation, a strategy pronounced by JCAHO in 2003. The most commonly identified problems were untreated indication, non-allergic adverse drug event, unnecessary

drug treatment and drug interactions which were caused by drug selection, inappropriate timing of administration and prescribing error. Factors associated with occurrence of DRPs include middle age, administering more than 10 drugs and in-hospital stay. Some of these DRPs were brought notice of the prescribers and eventually solved. Thus, the involvement of clinical pharmacist in conducting medical reconciliation will help ameliorate drug related discrepancies in transitions of care.

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#### **CONFLICT OF INTEREST**

Nil.

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