International Journal for Pharmaceutical Research Scholars (IJPRS)

V-4, I-1, 2015 ISSN No: 2277 - 7873

RESEARCH ARTICLE

Study of Prescribing Pattern of Fixed Dose Combinations in the Medicine Department of a South Indian Tertiary Care Teaching Hospital

Londhe SP [1,3*], Basavanagowda GM[2], Gowraw NS[2], Roopashree PM[2], Baishnab S[3]

[1]*Research Scholar, R. K. University, Rajkot, Gujarat, India.*

[2] *Sixth year Pharm D, Bapuji Pharmacy College, S.S. Layout Davangere-577004, India.*

[3]*Lecturer, Bapuji Pharmacy College, Davangere -577004, India.*

Manuscript No: IJPRS/V4/I1/00031, Received On: 28/02/2015, Accepted On: 08/03/2015

ABSTRACT

To study the prescribing pattern of fixed dose combinations in the medicine department of South Indian tertiary care teaching hospital. The study was a prospective, observational study. The study was conducted for a period of 6 months. Data required to study the prescription pattern was collected from the inpatient case sheets in the medicine department and subjected to assess the pattern of FDCs prescribed and also rationality of FDCs by using WHO and DCGI drug list. Among the 100 patient case sheets 284 FDCs were found. Out of 284 FDCs most commonly prescribed FDCs belonged to antimicrobial group 66(23%).

- 95(33.45%). FDCs prescribed without indications
- 31(10.91%) FDCs prescribed with inappropriate dose.

Out of 284 FDCs, 202(71.12%) FDCs were present in the DCGI list and only 4(1.40%) FDCs were present in the WHO essential medicine list. In this study most of the FDCs failed to meet the WHO guidelines. Most of the physicians are unaware of WHO and DCGI guidelines. Pharmaceutical manufacturer, however continue to produce huge amount of fixed dose combinations and continue promoting them with vigour. The DCGI should put tremendous pressure on pharmaceutical companies on withdrawal of irrational drugs from market as it affects a large number of drug units.

KEYWORDS

Fixed-Dose Combination, DCGI List, WHO Essential Medicine List, Rationality, Prescribing Pattern

INTRODUCTION

Fixed-dose combination is a combination of two or more active ingredients produced in a single dosage form. It may be administered as single entity products given concurrently or as a finished pharmaceutical product.[3]

***Address for Correspondence:**
Mr. Sushilkumar P Londhe
Research Scholar,
R. K. University,
Rajkot, Gujarat, India.
E-Mail Id: lsushil2002@gmail.com

The main advantages are:

- Increase in patient's compliance,
- Decrease in pill burden,
- Reduced complications
- Cost.

CDSCO approved FDCs

The Central Drugs Standard Control Organization (CDSCO) has issued a

comprehensive list of Fixed Dose Combinations (FDCs) drugs approved by Drugs Control General of India (DCGI) since 1961 till February, 2013. The list includes a total of 1125 FDCs covering all therapeutic categories.[11]

Focus on WHO Guidelines

The FDCs were termed as rational if they had.

- Active Pharmaceutical Ingredients with complementary mechanism of action.
- Decrease the occurrence of resistance for antimicrobial agents (AMA).
- Decrease the occurrence of adverse drug reactions or toxicity.
- Increase the compliance of the drug therapy with decrease pill burden.
- Dose of each API should be appropriate for defining a larger groups of populations.[1]

The FDC was termed as absurd if it shows

- No rationale or justification for combination.
- No increase in efficacy than individual drugs.

Disadvantages of FDCs

- Titration of dose of medicine to suit individual patients is not possible. E.g., atorvastatin 10 mg + amlodipine 5 mg.
- One of the drugs in the combination may be superfluous or wasteful. E.g., vitamins + iron.
- The incidence of adverse effects increases. E.g., nimesulide + paracetamol.
- It is difficult to identify which medicine in the FDCs has caused an adverse effect.[3]

National Scenario

According to Drug and cosmetic act 1940 (122E), every new FDCs should be considered as a new drug and should be allowed for marketing only after submission of relevant preclinical and clinical trial data. Rationality or irrationality of FDCs can be examined based on the provisions made in Schedule Y. The power of examination of a FDC lies with licensing authority mentioned under section 21(b) of Schedule Y.

It has been argued that many pharmaceutical companies have got marketing permission for Irrational fixed dose combinations from state licensing authorities, who are presently under the screening of DCGI and more importantly some banned FDCs are still being marketed. Broadly speaking it is difficult to stop the marketing of all the IFDCs but some measures should be taken to effectively prevent the same.

To reduce the confusion of licensing the marketing of IFDCs, WHO has formed guidelines in the 39th Report, 2005 on specifications for pharmaceutical preparations (WHO technical report series 929).If used it can help to reduce the flood of IFDCs. However, According to Schedule Y Appendix VI (b), such FDCs where active ingredients are already approved/marketed individually, reports of clinical trials carried out in the country should be submitted. When ratio of ingredients in approved FDCs is to be changed then also manufacturers need to submit clinical trial data to DCGI.[3]

Current Issues on Irrationality of FDCs in India

WHO model list of the essential medicine list contains only 18 approved drug combinations whereas in India, there are so many FDCs being marketed but not approved in developed country. Most of these combinations are not approved by DCGI and hence illegal.

DCGI controversial order to withdraw 1105 combination drugs from market seems to have lost transit. The order has not reached the drug controller so far. The decision to withdraw the combinations from the market was taken at the consultative committee meeting of state drug controllers convened last month in Delhi by DCGI. Once the product licenses are obtained from these badly administered states, the pharmaceutical companies are free to market these products throughout the country. These irrational combinations are freely available in states such as Maharashtra, Andhra Pradesh and Gujarat which usually disallows applications for such irrational combinations.[17]

Steps Taken by DCGI for Control on FDCs

The Drug Controller General of India is understood to be framing a broad policy document on fixed combinations to have an amicable way to settle the issues of weeding out irrational combinations from market. The directive to withdraw the listed combinations of drugs, which are not so far cleared by the national authority, placed the pharma firms on the conclusions with court stays and loud protests.

The Drug Controller General of India has directed the state drug controllers to follow a strategy in weeding out irrational drugs from the market. The DCGI has also directed to the state drug controllers not to give manufacturing licenses henceforth to FDC drugs without the approval of the DCGI office in Delhi. With the help of the pharmacologists, the DCGI has divided the 294 FDCs broadly into 3 categories. The first category consists of 120 combinations which are classified as banned, absurd and rejected. They are 16 absurd, 15 banned and 89 rejected. In the second category, there are 150 which need further examination. In the remaining 24 cases, 5 combinations are already approved.[17]

MATERIAL AND METHODS

Study Site

This study was conducted at a tertiary care teaching hospital in Davangere city.

Study Design

The study was a prospective, observational study.

Study Duration

The study was conducted for a period of six months from December 2013 to May 2014.

Inclusion Criteria

- Patients admitted in Medicine Ward.
- Patients aged more than 18 years.

Exclusion Criteria

- Patients aged less than 18years.
- Patients admitted other than medicine ward.
- Non-co-operative Patient.

Source of Data Collection

In patient's case sheets.

Ethical Approval

This study was approved by Institutional Ethical Committee.

Data Collection Form and Study Procedure

A suitably designed patient data collection form was developed. The collected data of the FDCs were documented in patient data collection form. The investigators attended the ward rounds, followed-up the patients every day and collected entire details about the drug therapy from the case sheets which contained at least one FDC and filled in patient data collection form. The data was collected every day for a period of 6 months and were analysed. The number of FDCs prescribed in each prescription was taken into account to analyse the pattern of FDCs prescribed, to make categorization, to find out rationality and comparing with WHO and DCGI guidelines.

RESULTS

Gender

A total of 100 patient case sheets were collected out of which 55(55%) were male and 45(45%) were female**.**

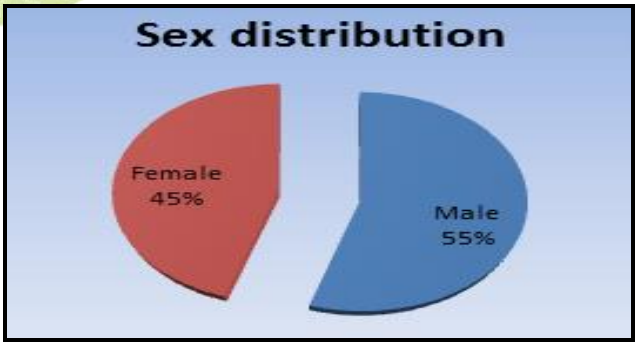

Figure 1: Distribution of cases according to gender

Number of FDCs Found in the Total Medications of Patients

A total 100 patient case sheets were collected and analysed for total FDCs in medication chart of patient case sheets.

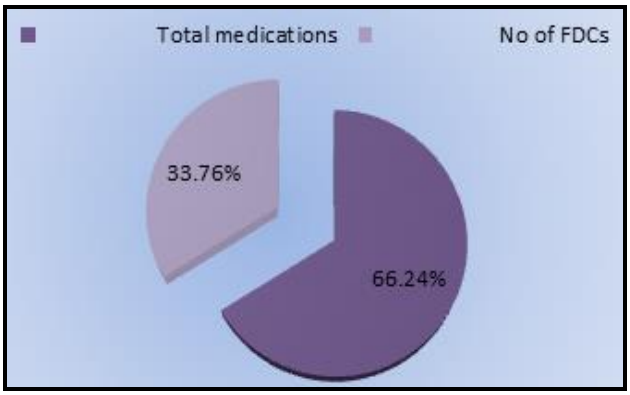

Figure 2: Number of FDCs found in the total medications of patients

Number of Cases According to Age Group (n=100)

A total of 100 patient case sheets were collected and they were assigned according to age criteria.

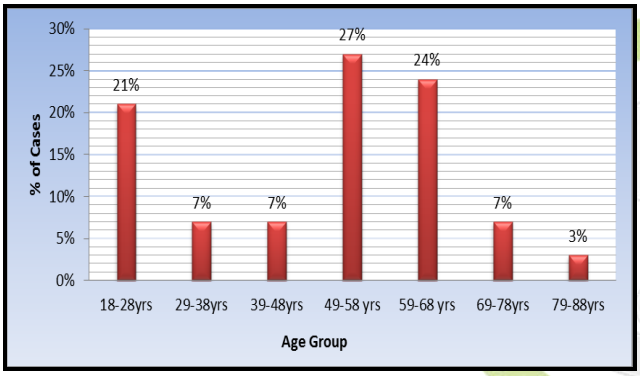

Figure 3: Number of cases according to age group (n=100)

Number of FDCs Prescribed in Particular Age Group

A total of 100patient'scase sheets were collected and were analysed for the number of FDCs prescribed in the following age groups.

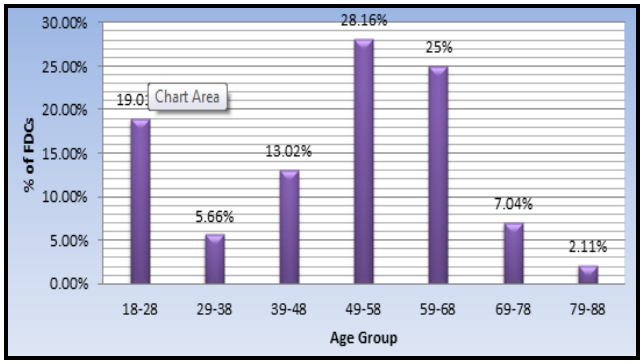

Figure 4: Number of FDCs prescribed in particular age group

Number of FDCs Found in Past Medication History of the Patient Case Sheets

A total 100 patient case sheets were collected and analysed for number of FDCs in past medication history in the patient case sheets.

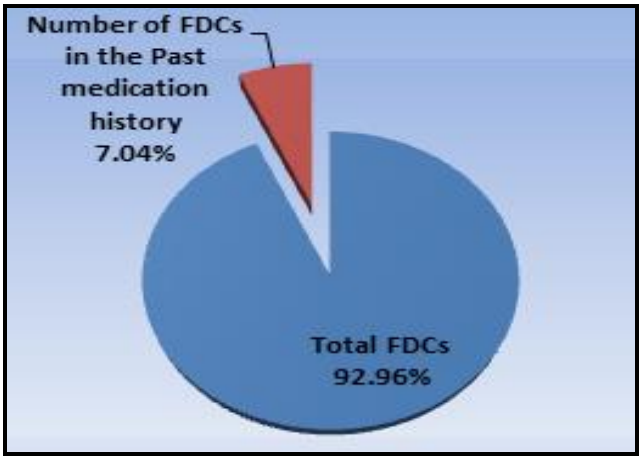

Figure 5: Number of FDCs found in past medication history of the patient case sheets

Number of FDCs Repeatedly Found in Patient Case Sheets

A total 100 patient case sheets were collected and analysed for number of FDCs repeatedly found in case sheets.

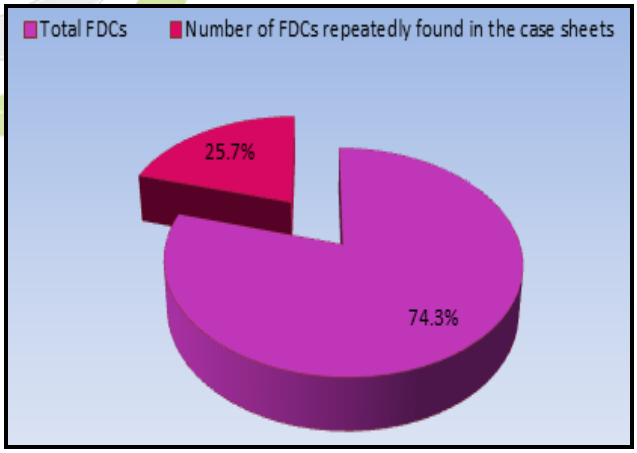

Figure 6: Number of FDCs repeatedly found in patient case sheets

Categorization of FDCs According to Pharmacological Action

A total 100 prescriptions were collected and analysed for categorisation of FDCs according to pharmacological action.

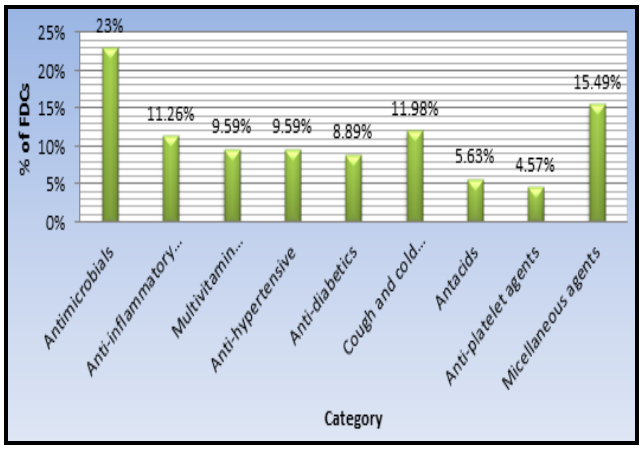

Figure 7: Categorization of FDCs according to pharmacological action

Number of FDCs Prescribed with Right Indication

A total of 100 patient case sheets were screened which contained 284 FDCs out of which 189(66.54%) FDCs were given for the right indication. Remaining 95(33.45%) FDCs were prescribed without indication.

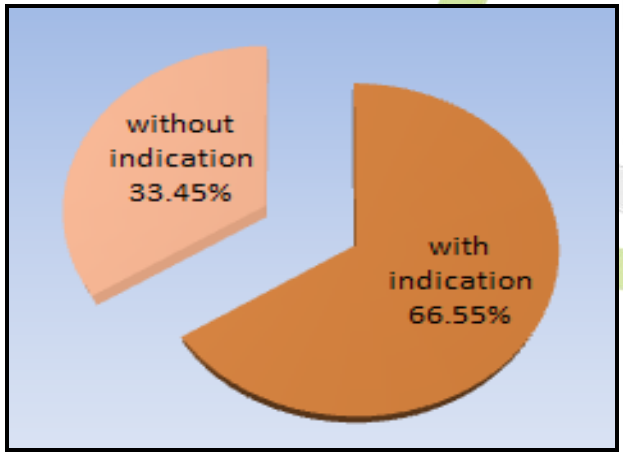

Figure 8: Number of FDCs prescribed with right indication

Number of FDCs Prescribed with Right Dose

A total of 100 patient's case sheets were screened out of 284 FDCs, 253 FDCs were prescribed with the right dose and remaining 31 FDCs were prescribed with inappropriate dose.

Rationality of FDCs According to DCGI and WHO List

A total of 100 patient's case sheets were screened out which contained 284 FDCs. Out of 284 FDCs 202(71.12%) FDCs were present in the DCGI list and only 4 FDCs (Isoniazide + Rifampicin, Levodopa + Carbidopa, Ferroussalt + Folicacid, Amoxicillin + Clavulanic acid) present in WHO essential drug list. Remaining 78(27.48%) FDCs were not present in both DCGI and WHO drug list.

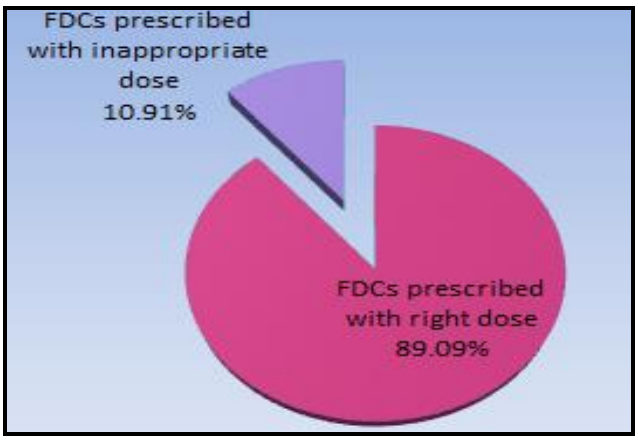

Figure 9: Number of FDCs prescribed with right dose

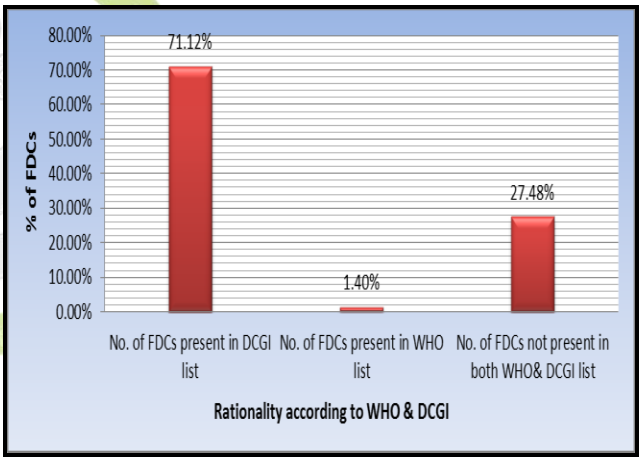

Figure 10: Rationality of FDCs according to DCGI and WHO list

DISCUSSION

Inappropriate and indiscriminate use of FDCs is a global problem causing selection of resistant strains which has resulted in a substantial economic burden on individual and health care system. There are many popular FDCs in the Indian pharmaceutical market, which have flourished in the last few years. The Indian drug control authority has issued notifications banning many FDCs. For this it is very prudent to study the prescribing pattern of FDCs in medicine department.

The study was conducted for a period of 6 months and data was collected in prospective series of inpatients in medicine department who are prescribed with FDCs. A total of 100 patients met the inclusion criteria.

After considering the inclusion and exclusion criteria the medicine department was selected. After receiving the ethical clearance from the institute of ethical committee the data collection was initiated.

A total of 100 patient's case sheets were analysed during the study out of which, 55 (55%) were male and 45(45%) were Female. This study also revealed a male predominance over female as similar to a study conducted by Laveesh M.R et.al showed that 540 patients were evaluated. It consisted of 298(55.18%) males and 242(44.81%) females.

The study focused on the patients who are aged more than 18yrs and majority of the patients were in the age group of 56- 60 yrs. Since this age group usually has much inter-current illness, they might be subject to poly-pharmacy which increases the chance for prescribing FDCs.

100 patients were screened during the study period after considering the inclusion and exclusion criteria from medicine department of tertiary care teaching hospital in Davangere city. 100 patient case sheets were collected and analysed for pattern of FDCs prescribed. 100 case sheets contain total 284 fixed-dose combinations out of which 202 (71.12%) of FDCs were present in the DCGI list and remaining 82(28.87%) of FDCs were outside the list. 2013th DCGI list contains 1125 FDCs. 18th WHO essential medicine list(EML) of 2013 contains only 24 FDCs. In this study, there were 98.59% FDCs which were outside the list of FDCs in WHO essential medicine list and were not according to WHO criteria towards rational FDCs. The study has similar findings with the study conducted by Jain N.K, et.al in which out of 225 FDCs only 45(20%) recommended by the WHO list.

A total 284 FDCs were collected and categorised based on their pharmacological actions. In our study majority of the most commonly prescribed FDCs were antibiotics 66(23%) followed by cough and cold preparations 34(11.97%). Ceftriaxone and sulbactam combinations are most commonly prescribed antibiotic FDCs. The study has similar findings with the study conducted by Rayasam S.P et.al shows antibiotics were most commonly prescribed. It was also found that there was a trend towards prescribing antimicrobial FDCs for common ailments like upper and lower respiratory tract, urinary tract and gastro-intestinal tract infections. These findings are in accordance with the study conducted by Laveesh M.R et.al found that out of 540 prescriptions collected from medicine OPD, 25.37% prescriptions contained antimicrobial agents. The prescribing pattern of the present study was found to be similar to those observed in the previous studies.

Total number of drugs (including single as well as combination) found in 100 patient's case sheets were 841 drugs. Out of 841 drugs the numbers of FDCs were found to be 284(33.76%). The past medication history of the patient were also collected and the number of FDCs found in the past medication history were 20. Out of 284 FDCs, 73(25.70%) FDCs were repeatedly prescribed in the medication chart.

A total of 100 patient's case sheets were screened out which contains 284 FDCs out of which 189(66.54%) FDCs are given for the right indication. Remaining 95(33.45%) FDCs are prescribed without indication.253 FDCs were prescribed with the right dose and remaining 31 FDCs were prescribed with inappropriate dose. It shows clear objective to prescribe FDCs with correct dose and indication, considering appropriate information to the patient. Our study had similar findings with the study conducted by Rayasam S.P et.al which showed that 80% of FDCs did not confirm rationality based on indication and dose criteria.

Nonetheless, these results indicate a considerable scope for improving the prescribing pattern of drugs in medicine department. The improvement would be facilitated by providing feedback,

prescriber education and creation of a hospital formulary.

CONCLUSION

All the results of the study clearly show an urgent need to follow prescribing pattern for a longer period and to formulate and implement contextually appropriate prescribing guidelines based on local prescribing. Choice of combinations depends upon the risk factors, presence of co-morbidities, adverse effects and tailored according to individual patient.

In this study most of the FDCs failed to meet the WHO guidelines. Overall, Most of the physicians are unaware of WHO and DCGI guidelines. Pharmaceutical manufacturer, however continue to produce huge amount of fixed dose combinations and continue promoting them with vigour. Most of the state-level drug authorities often taken advantage from pharmaceutical companies who push irrational combinations without proper security. The DCGI should put tremendous pressure on pharmaceutical companies on withdrawal of irrational drugs from market as it affects a large number of drug units.

REFERENCES

1. Rayasam, S. P., Dudhgaonkar, S. S., Dakhale, G. N., Hire, R. C., Deshmukh, P. S., & Gaikwad, N. N. (2013). The irrational fixed dose combinations in the Indian drug market: an evaluation of prescribing pattern using WHO guidelines. *International Journal of Basic & Clinical Pharmacology*, *2*(4), 452-457.
2. Rathnakar, U. P., Shenoy, A., Ullal, S. D., Sudhakar, P., Shastry, R., & Shoeb, A. (2011). Prescribing patterns of fixed dose combinations in hypertension, diabetes mellitus and dyslipedimia among patients attending a cardiology clinic in a tertiary care teaching hospital in india. *International Journal of Comprehensive Pharmacy*, *2*(6), 1-3.
3. Raut, S., Dhone, P., Pise, N., Verma, R., Gupta, R. K. (2012). Current Pattern of Use Irrational Fixed Dose Combinations: A Prescription Audit Study. *Research Journal of Pharmaceutical, Biological and Chemical Sciences, 3*(4), 617-22.
4. Manjula Devi, A. S., Sriram, S., Rajalingam, B., Alfet Raju, A., Varghese, R. S., & Venkata Phani, A. (2012). Evaluation of the rationality of fixed dose combinations of cardiovascular drugs in a multispecialty tertiary care hospital in Coimbatore, Tamilnadu, India. *Hygeia J. Drugs Med.*, *4*, 51-58.
5. Maladkar, M., Verma, V. K., Narsikar, K. A., Walinjkar, R. D., Patil, W. R., Saggu, N. J. S., & Kulkarni, S. P. (2012). Triple drug combination of telmisartan, amlodipine and hydrochlorothiazide in the treatment of essential hypertension. *Open Journal of Internal Medicine, 2*(1), 67-71.
6. John, L. J., Devi, P., John, J., & Guido, S. H. O. B. A. (2011). Drug utilization study of antimicrobial agents in medical intensive care unit of a tertiary care hospital. *Asian Journal of Pharmaceutical and Clinical Research*, *4*(2), 81-4.
7. Vijayakumar, T. M., Poovi, G., Swaroop, T. V., Thirumurujan, G., Dhanaraja, M. D. (2010). Prescribing pattern of fixed dose combinations focus on cardiovascular drugs in out -patient department of Private Hospital. *Journal of Pharmacology and Toxicology*.
8. Laveesh, M. R., et al. (2013). Prescription audit of antimicrobials in the medicine outpatient department of a tertiary care hospital. *International Journal of Pharmaceutical and Biomedical Research*, *4*(3), 177-80.
9. Mweemba, W. (2011). Evaluation of the Quality of Fixed Dose Combination Anti Tuberculosis drugs in public and private health institutions in Lusaka District. *Medical Journal of Zambia, 38*(3), 16-21.
10. Saeed, S., Saeed, P., Sharma, V. (2012). Current scenario of rational usage of various drugs in indoor patients. *International Journal of Basic and Clinical Pharmacology, 1*(1), 27-32.

11. Fortin, A., Verbeeck, R. K., Jansen, F. H. (2010). Comparative oral bioavailability of non-fixed and fixed combinations of artesunate and amodiaquine in healthy Indian male volunteers. *Springer Publication, 6*(7), 267-275.

12. Kalra, S., Kalra, B., Agarwal, A. (2010).Combination therapy in hypertension: an update. *Biomed Central Journal*, (2), 1-11.

13. Sharma, M., Eriksson, B., Marrone, G., Dhaneria, S., Lundborg, C. S. (2012). Antibiotic prescribing in two private sector hospitals; one teaching and one non-teaching: Across-sectional study in Ujjain, India. *Biomed Central Journal*, (12), 1-9.

14. Laveesh, M. R., et al. (2013). Prescription audit of antimicrobials in the medicine outpatient department of a tertiary care teaching hospital. *International Journal of Pharmaceutical and Biomedical Research, 4*(3), 177-180.

15. Jain, N. K., et al. (2009). Rationality of fixed dose combinations: an Indian scenario. *The Pharma research*, (1), 158-168.

16. Garg, K., Verma, V., Kumar, S. (2012). Fixed dose combination of telmisartan and hydrochlorthiazide: is it totally safe. *International Journal of Pharma and Bio Science*s, (3), 201-203.

17. Shirure, P. A., Tadvi, N. A., Bajait, C. S., Baig, M. S., Gade, P. R. (2012). Comparative effect of fixed dose combination of Amlodipine + Bisoprolol versus Amlodipine and Bisoprolol alone on blood pressure in stage-2 essential hypertensive patients. *International Journal of Medical Research and Health sciences*, (1), 13-19.

18. Pan, F., Chernew, M. E., Fendrick, A. M. (2008). Impact of fixed-dose combination drugs on adherence to prescription medications. *Journal of General Internal Medicine, 23*(5), 611-614.

19. Bell, N. P., Ramos, J. L., Feldman, R. M. (2010). Safety, tolerability, and efficacy of fixed combination therapy with dorzolamidehydrochloride 2% and timolol maleate 0.5% in glaucoma and ocular hypertension. *Dove Medical Press*, (4), 1331-1346.

20. Shiga, Y., et al. (2012). Efficacy and safety of a single-pill fixed-dose combination of high-dose telmisartan/hydrochlorothiazide in patients with uncontrolled hypertension. *Journal of Renin-Angiotensin- Aldosterone System*, 394-400.

ANNEXURE-I

DATA COLLECTION FORM

Patient Name	
Age	
Sex	
Date of Admission	
Date of Discharge	
Present Complaints	
Past Medical History	
Past Medication History	
Diagnosis	

Medication Chart

Medication	Generic Name	Dose	Frequency

Analyse the medication chart for the following

Number of fixed dose combinations found	
Compare the FDCs with WHO and DCGI list	
Drug category	
Rationality	

Report:-