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Pharmacoepidemiology and Drug-Drug interactions in various regions of Andhra Pradesh

Bothiraj M*[1], Alagusundaram M[2], Chandra Sekhar K.B[3]

[1]Research scholar, Jawaharlal Nehru Technological University, Ananthapuramu, Andhra Pradesh, India
[2]Jagan's College of pharmacy, Nellore, Andhra Pradesh, India
[3]Krishna University, Machilipatnam, Andhra Pradesh, India

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ABSTRACT

Pharmacoepidemiology deals with the use and effects of medications in a large number of population—the combination of epidemiology principles to the effects of drug and its usage. Pharmacoepidemiology helps in optimal utilization of medicines and assist health care providers in making better decisions on drug therapy that will tend to curtail the Drug-Drug interactions, thereby prevents alteration in the pharmacological activity of one drug by another. Among all types of interaction, Drug-Drug interaction causes a higher rate of mortality. A prospective study conducted with 653 prescriptions that were collected from the various regions of Andhra Pradesh like Kadapa, Proddatur, Pulivendula, Kurnool are checked in interaction checker, results are projected in 4 categories a) Age and Sex preponderance(Demographics) rate of drugs interaction b) Interaction rate of major/minor type c) Department wise - General medicine (72.37%), Gynaec (69.02%), Pediatric (29.33%), Ophthalmology (75%) d) Most common interacting pairs of various department Ex: Ceftriaxone & Furosemide, Diclofenac & Furosemide, Albuterol & Losartan are observed in General Medicine. Statistical significance (P-value 0.00002) is obtained based on One Way ANOVA. This study elucidates the significance of pharmacoepidemiology; however, this requires much efforts to prevent causation effects of drugs. It is helpful to locate them by the establishment of "Drug interaction monitoring program" or by establishing "Pharmacoepidemiological centres" in every hospital for the screening of prescriptions by *"Pharmacist"* and thereby edify doctors and public for better medication use.

*Corresponding Author

Name: Bothiraj M
Phone: +91 9382782707
Email: bothi.pharm@gmail.com

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INTRODUCTION

Pharmacoepidemiology deals with the use and effects of medications in a large number of population (Maklan *et al.*, 1994). It includes clinical pharmacology and epidemiology. It applies the epidemiology principles with drug use and effects (Strom, 1994). Study information is gathered and analyzed to identify possible causation and related factors that can be applied in clinical practice to groups of people and also individuals undergoing treatment. Pharmacoepidemiology studies the relativity between exposed drug and health outcomes in identified (Wettermark, 2013). Pharmacoepidemi-

ological studies aimed at quantifying risk and anticipate ways of Type A effects and lessen the risk by discerning the predisposing factors and enhanced dosing guideline. Type B ("bizarre") effects are not expected due to anticipated pharmacological features of a drug in suggested doses who metabolize the drug in the usual way (Stockley, 2002). Drug-Drug interaction is the alteration of the drug effect by another drug, food or herbal constituents' (Vonbach, 2007).

Drug interactions are categorized based on mechanism, pharmacokinetic and pharmacodynamic interactions. Drug interactions have to consider both new drugs (investigational drug) and already approved drugs that are administered as co drug. On requirement, the clinical or non-clinical drug interaction studies to be initiated to determine the possibility of drug interactions and to measure their influence on drug therapy (Porta and Hartzema, 1991). A prospective study carried out intending to identify the unintended effects that are associated with the prescriptions; those were collected from various regions of Andhra Pradesh.

1. Epidemiological distribution of drug-drug interacted prescriptions.
2. Drug-drug interactions rate in the collected prescriptions.
3. The most commonly interacted drug pairs in total prescriptions.
4. To explore the most severe interacted drug pairs.
5. To check whether the drug interaction occurred by chance is the significance (or) non-significance.

MATERIALS AND METHODS

Collection of Prescriptions

A prospective study performed by collecting floating prescriptions in various areas like Kadapa, Anantapur, Kurnool, and Pulivendula on consent from the retail pharmacist to note the prescribed drugs in the prescription at many retail pharmacy shops for six months and collected drug therapy details with 110 patients. Drug interaction screening intervention programs are a paramount tool to discern prescriptions of several drugs for potential drug-drug interactions (pDDIs). Many programs are present on the market. They differ in layout, update frequency, search functions, content and price. The current study aimed to critically appraise interaction screening programs in the Andhra Pradesh Patients (Corder and Foreman, 2009). Those treated with various drugs for various diseases are taken into consideration. Patients were categorized according to their age (Parthasarathi *et al.*, 2012), type of disease, and interactions are grouped based on department wise as General Medicine, Gynaec, Pediatric and Ophthalmology. The study period of June 2011 to December 2011 with inclusion (at least two drugs) and exclusion criteria(Severe illness). Following patient enrollment, baseline information of patient name, age and clinical presentation & diagnosis is recorded. The collected prescription was checked using drug interactions checker. Epidemiology is a basic science to enhance the quality health of people and mainly the health of the disadvantaged (Armitage and Colton, 2005). This prospective observational study elucidates those who consume the medication in excess or without any knowledge on administration paves to unintended effects (Hennekens *et al.*, 1996).

Segregation of the prescriptions

After collecting the total Prescriptions, the same segregated as per the department wise interactions. The four significant departments listed are:

1. General medicine
2. Gynaecology
3. Paediatrics
4. Ophthalmology

In this exploration, the selection of study samples and the scaling of exposures and outcomes (Sackett, 1979) are correlated.

Screening for Interactions

The collected prescriptions are carefully screened for Drug-Drug Interactions through Tertiary interaction references like Medscape, Drug-Drug Interaction checker software. First, a systematic review and identification of significant drug interactions in tertiary drug interaction references, including drug interaction evaluation with facts and Multidrug interaction checker (www.medscape.com). In this study, all the comparisons were made within the study base (Wacholder *et al.*, 1992).

The drug interaction checker reflects potential drug interaction, shares an inference on pharmacological mechanisms of the interaction (pharmacokinetic, pharmacodynamic, or unknown) and classification based on severity level and substantiating scientific evidence. The Multidrug interaction checker software possesses both sensitivity and specificity to

97% in discerning drug combinations with interaction potential. A list of all selected 'major' interactions was developed.

Rate of Interactions

After determining the entire Drug-Drug interactions in the total prescriptions, the rate of interactions in each department for total prescription was calculated.

Application of the Statistics

The statistics were applied by using Intel Instant graph pad software to test the significance.

Kruskal-Wallis one-way analysis of variance

It is used to compare more than two samples those are independent, or not related. It is the one-way analysis of variance (ANOVA). The factual null hypothesis is that the populations, from which samples originate and have the same median. This test leads to significant results, later at least one of the samples is different from the other samples. Because it is a nonparametric tool, the test does not assume a normal distribution, not like the equivalent way analysis of variance. However, the assessment does assume a similarly-shaped and scaled prevalence for each group, except for any variance in medians (Taylor, 1982). The exploration illustrates projected epidemiologic theory with examples from various biological settings (Steineck and Ahlbom, 1992).

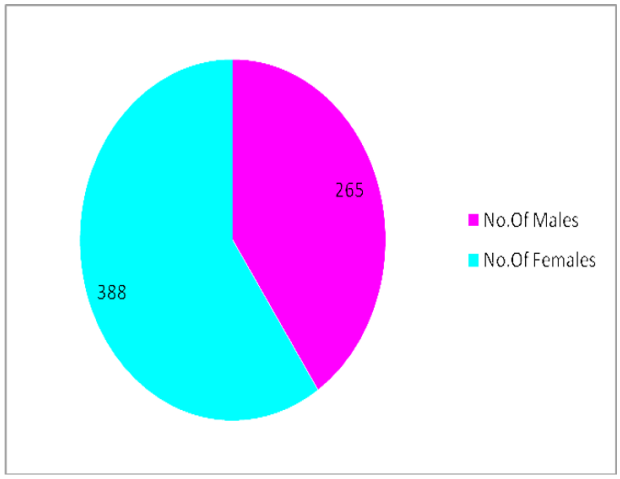

Figure 1: Number of males vs. females

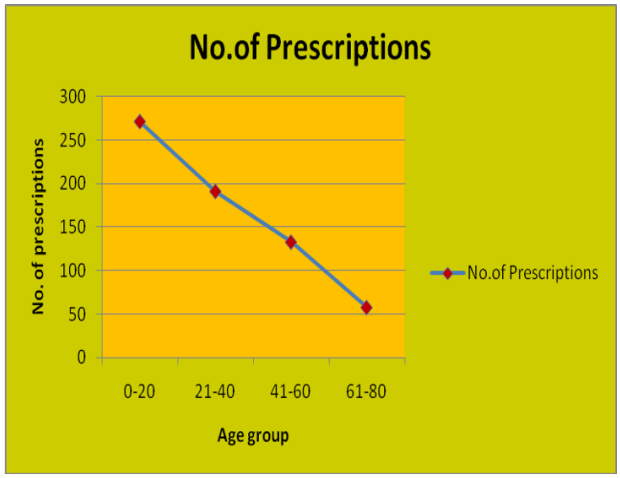

Figure 2: Number of Prescriptions Vs Age

RESULTS AND DISCUSSION

In this prospective study, the collected 653 prescriptions from the various regions of Andhra Pradesh like Kadapa, Proddatur, Pulivendula, Kurnool has shown the drug interaction, which is as follows.

1. Demographic – Age & Sex
2. Interaction severity – Major/Minor
3. Department wise – interaction
4. Most commonly interacting pairs

The distortion of the age and sex spreadability and the clinical vulnerability of disease can even affect judgments about the optimal interactions while among the medical care (Melton, 1985).

Gender Distribution

Figure 1 reveals that 265 were males and 388 were female patients out of 653 patients.

Age Distribution

Table 1 shows the dispersion of recruited patients for the study in various age groups. The maximum number of patients 271 were found to be in the age group of 0-20 years, and 191 patients belong to the age group of 21-40 years. Only 58 patients were at the age group of 61-80 years, whereas 133 patients were present in the age group of 41-60 years.

The number of prescriptions with interactions with an age range of Patients were depicted in Figure 2. The prescriptions containing two or more drugs have the highest potential drug interactions aged 0-20 years.

Interaction – Major/Minor

There were in total 653 prescriptions, of which all were poly pharmacy with two or more drugs, that is considered to possess a risk of drug interactions. Many prescriptions (257) were from the General Medicine department.

Possible drug interactions discerned within one prescription presented as either the number of interacting drug pairs and numbers of interactions with prescription are at a significant level. There was a total of 749 drug interacting pairs in 653 pre-

Table 1: Age pattern of patients

Age (years)	No. of Patients	%
0-20	271	41.50
21-40	191	29.24
41-60	133	20.36

Table 2: Department wise number of interacting pairs & its rate

Department	No. of interacting pairs	No. of prescriptions with interactions	Rate of interacted pairs %
Paediatric	60	44	8
General Medicine	457	186	61
Gynaecologist	203	156	27.1
Ophthalmologist	29	15	3.8

Table 3: Most commonly interacted drug pairs

Name of drugs	No. of times	Percentage
Ceftriaxone+Furosemide	74	31.5%
Albuterol+Furosemide	10	4.23%
Amoxicillin+Ceftriaxone	17	7.20%
Diclofenac+Furosemide	16	6.77%
Phenytoin+Diazepam	11	4.66%
Metronidazole+Diclofenac	17	7.20%
Ceftriaxone+Diclofenac	44	18.64%
Ranitidine+ Phenytoin	21	8.89%
Atenolol+Amlodipine	19	8.05%
Atropine+Pralidoxime	2	0.84%
Enalapril+Furosemide	11	4.66%
Ceftriaxone+Cefotaxime	24	10.16%

scriptions. 346 drug interacting pairs were labelled as major interactions. The compiled rate of potential to interact drugs was 61.4%. Those of the main level accounted for 46.19%. The most significant usual interacting drug pair was Ceftriaxone + Furosemide (74 prescriptions), while the second common was Ceftriaxone + Diclofenac involving 44 prescriptions. Major interactions were prominent in the Department of General Medicine (125 prescriptions). The clinical pharmacist recommended alternatives (Primejdie *et al.*, 2014) to reduce the incidence of DDIs to reverse the interaction listed in Table 2.

These potential DDIs were identified as a drug-related problem (Lau *et al.*, 2005) in the present study. Concerning all instances of inappropriate drugs use, resembled other similar studies (Halvorsen *et al.*, 2010). The hospital eventuality model should be applied with extreme precaution to evaluate hospital quality of care (Ballard *et al.*, 1994) which is the reflection of a drug-drug interaction.

Department wise drug interactions

The rate of interactions are high in the department of general medicine (61%), followed by gynaecology (27.1%), pediatric (8%) and less in the ophthalmic department (3.8%).

General medicine

Out of 257 prescriptions in general medicine, 163 prescriptions belongs to males, and remaining 94 prescriptions belong to females. 186 prescriptions have unlikely drug interactions. The percentage of interactions occurred by chance was found to be 72.37%.

Gynaec Department

In the Gynaec department total, number of prescriptions is 226. In this unlikely drug interaction occurrence by chance was found to be 69.02%.

Pediatric Department

The total number of prescription in this department was found to be 156. The unlikely drug interaction was found to be 29.33%.

Ophthalmology

A total number of prescriptions found to be 20. The percentage of interaction occurred by chance was found to be 75%.

Interactions commonly observed in departmental wise

Table 3 elaborates that among all the drugs Ceftriaxone & Furosemide, Diclofenac & Furosemide, Albuterol & Losartan frequently interacted in General Medicine Department.

In Gynaec Department Ceftriaxone & Diclofenac, Atenolol & Amlodipine, Amoxicillin & Ceftriaxone interacted commonly.

In Pediatrics Department Phenytoin & Ranitidine, Ampicillin & vitamin k interact commonly.

In Ophthalmology Department Ceftriaxone, Cefotaxime, Diclofenac interacted.

Based on the above information statistics was applied to find unlikely drug interaction that occurred by chance is statistically significant or non-significant by using the Intel instant Graph Pad and found that study is extremely significant by the produced p-value 0.00002.

The strong correlation between the use of inhaled beta two agonists and mortality of asthma patients are confined to the use of drugs above recommended limits (Crane *et al.*, 1995). Similarly, the potential interaction is due to the excess or non-Compliance of the prescription schedule.

CONCLUSION

The study results demonstrate the need for vigilant measures, the intervention of pharmacist in the prevention and detection of drug interactions. The pharmacist provides accurate advice on optimum drug usage based on the skills of drug interaction, that can significantly add to patient safety and well-being. The establishment of "Drug Interaction Monitoring Program" or by establishing "pharmacoepidemiological centres" in every hospital for proper screening of the drug interactions, to avoid adverse drug reactions while dispensing the medicines by *"Pharmacist"* and that demonstrates the need to elucidate the doctors and public, which will lead to better use of medication. But in future, more recognition and research work will be required to make Pharmacoepidemiological programs to succeed in preventing or minimizing drug interactions.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

REFERENCES

Armitage, P., Colton, T. 2005. Encyclopedia of Biostatistics. Wiley. Volume 8, Second Edition, ISBN: 978-0470849071.

Ballard, D., Bryant, S. C., Brien, D. 1994. Referral selection bias in the Medicare hospital mortality prediction model: are centers of referral for Medicare beneficiaries necessarily centers of excellence? *Health Services Research*, 28(6):771–784.

Corder, G. W., Foreman, D. I. 2009. Nonparametric Statistics for Non-Statisticians: A Step-by-Step Approach. Wiley. First Edition, ISBN: 978-0470454619, Pages 264.

Crane, J., Pearce, N., Burgess, C., Beasley, R. 1995. Asthma and the beta agonist debate. *Thorax*, 50(Suppl 1):S5–S10.

Halvorsen, K. H., Ruths, S., Granas, A. G., Viktil, K. K. 2010. Multidisciplinary intervention to identify and resolve drug-related problems in Norwegian nursing homes. *Scandinavian Journal of Primary Health Care*, 28(2):82–88.

Hennekens, C. H., Buring, J. E., Manson, J. E., Stampfer, M., Rosner, B., Cook, N. R., Belanger, C., LaMotte, F., Gaziano, J. M., Ridker, P. M., Willett, W., Peto, R. 1996. Lack of Effect of Long-Term Supplementation with Beta Carotene on the Incidence of Malignant Neoplasms and Cardiovascular Disease. *New England Journal of Medicine*, 334(18):1145–1149.

Lau, D. T., Kasper, J. D., Potter, D. E. B., Lyles, A., Bennett, R. G. 2005. Hospitalization and Death Associated With Potentially Inappropriate Medication Prescriptions Among Elderly Nursing Home Residents. *Archives of Internal Medicine*, 165(1):68–74.

Maklan, C. W., Greene, R., Cummings, M. A. 1994. Methodological Challenges and Innovations in Patient Outcomes Research. *Medical Care*, 32(Suppl 7):JS13–JS21.

Melton, L. J. 1985. Selection Bias in the Referral of Patients and the Natural History of Surgical Con-

ditions. *Mayo Clinic Proceedings*, 60(12):880–885.

Parthasarathi, G., Nyfort-Hansen, K., Nahata, M. C. 2012. A Textbook of Clinical Pharmacy Practice. Himayatnagar, Hyderabad. Universities Press. Chapter 24, ISBN: 9788173717567, page 408.

Porta, M. S., Hartzema, A. G. 1991. The contribution of epidemiology to the study of drugs. In *Pharmacoepidemiology: An Introduction*, Ohio. Harvey Whitney Books. Second Edition, Pages 2-17.

Primejdie, D. P., Mallet, L., Popa, A., Bojita, M. T. 2014. Description of a systematic pharmaceutical care approach intended to increase the appropriateness of medication use by elderly patients. *Medicine and Pharmacy Reports*, 87(2):119–129.

Sackett, D. L. 1979. Bias in analytic research. *Journal of Chronic Diseases*, 32(1-2):51–63.

Steineck, G., Ahlbom, A. 1992. A Definition of Bias Founded on the Concept of the Study Base. *Epidemiology*, 3(6):477–482.

Stockley, I. H. 2002. Stockley's drug interactions. London, Chicago. Pharmaceutical Press. Sixth Edition, ISBN: 978-0853695042, Pages 960.

Strom, B. L. 1994. What is Pharmacoepidemiology? In *Pharmacoepidemiology*, New York. Wiley. Second Edition, Chapter 1, ISBN: 9780471940586, Pages 3-13.

Taylor, J. 1982. An Introduction to Error Analysis. Sausalito, California. University Science Books. Second Edition, ISBN: 0935702423. Pages 327.

Vonbach, P. 2007. Drug-Drug Interactions in the Hospital. Inaugural dissertation, University of Basel, zürich.

Wacholder, S., McLaughlin, J. K., Silverman, D. T., Mandel, J. S. 1992. Selection of Controls in Case-Control Studies. *American Journal of Epidemiology*, 135(9):1019–1028.

Wettermark, B. 2013. The intriguing future of pharmacoepidemiology. *European Journal of Clinical Pharmacology*, 69(S1):43–51.