CHAPTER 2
LITERATURE REVIEW

1. Poorwa Wandalkar et al., (2015) conducted a prospective study on the “prevalence of potential drug interactions in medicine wards at a tertiary hospital”. Medscape drug interaction checker was used for analysis of the potential drug-drug interactions and about 638 potential drug-drug interactions were observed among 200 prescriptions. Most of the interactions were found to be in the age group 41-50 years when compared to the other age groups. Majority of the interactions were of minor severity (53%) and the remaining were of moderate (40.7%) and severe (6.3%). In this study, Octreotide + Ondansetron, Ranitidine + Ferrous Sulfate were the most common interacting pairs. The authors finally concluded that most of the interactions were preventable and the knowledge regarding the drug interactions can help the prescribers to prevent the concomitant use of dangerous drug combinations 

2. Sainul Abideen et al., (2015) conducted a study on the “assessment of prevalence of potential drug-drug interactions in medical intensive care unit (MICU) of a tertiary care hospital in India”. This is a retrospective study conducted for a period of 3 months and Lexi Comp drug interact android application was used for screening of drug interactions. About 72 patients were included in the study out of which 47 were males and 25 were females. At least one potential DDI was observed in 65 (90%) patients. About 222 interactions were found in the study with an occurrence rate of 3.08 DDI per patient. Majority of the interactions were of moderate severity (65.77%). Dopamine + Noradrenaline, Adrenaline + Sodium bicarbonate, Hydrocortisone + Ofloxacin and Dexamethasone + Sodium bicarbonate were found to be the most common interacting pairs observed. Finally, the authors concluded that the concomitant administration rate of potentially interacting drugs are very high in medical intensive care unit and to prevent and monitor
DDIs, special safety measures must be followed by physicians, pharmacists and nurses in all the departments of the hospital \[1\].

3. **Haftay Berhane Mezgebe et al., (2015)** conducted a study to determine the “prevalence of potential drug-drug interactions among the psychiatric patients”. This is a retrospective cross sectional study and the drug charts were reviewed and analyzed for potential drug-drug interactions using Micromedex online drug reference. A total of 216 cases were reviewed for potential drug-drug interactions. Among them, a total of 463 potential DDIs were detected. At least one potential DDI was observed in 81% of the patients. Majority of the interactions were of moderate severity (50.1%). The most frequent drug combination was observed to be Haloperidol and Trihexphenidyl followed by Chlorpromazine and Haloperidol. The authors predicted that majority of the interactions involved in this study may cause QT prolongation and cardiotoxicity. Close monitoring is required for the patients with polypharmacy and cardiovascular comorbidities \[52\].

4. **Bozana Nikolic et al., (2014)** conducted a cross sectional study to estimate the “prevalence of potential drug-drug interactions among the out patients along with the investigation of the predictors of potential DDIs”. A total of 4467 prescriptions were screened, out of which 1488 patients were exposed to 2558 significant potential DDIs. Based on “Drug Interactions Facts” by David S Tatro, all the drug combinations with potential for clinically significant DDIs were identified. The authors concluded that approximately one third of the out patients were exposed to potential DDIs and Sulfonyl ureas + Angiotensin Converting Enzyme (ACE) inhibitors and Potassium sparing diuretics + ACE inhibitors were the most common drug combination classes observed in this study \[14\].

5. **Kumara Swamy RC et al., (2014)** conducted a prospective study on the “prevalence of polypharmacy and drug-drug interactions in a tertiary care teaching hospital”. For the analyzation of treatment regimen, Micromedex,
Stockley’s drug interactions and Medscape drug interaction checker were used. A total of 940 prescriptions were screened and among them 480 prescriptions were with major polypharmacy followed by 216 were with minor polypharmacy and the remaining 244 prescriptions were with no polypharmacy. Majority of the patients were observed with respiratory disorders followed by cardiovascular diseases. Among these total prescriptions, 512 (54.46%) prescriptions were found to be with drug-drug interactions. About 734 drug-drug interactions were observed among these prescriptions and about 304 interactions were observed to be minor, 307 were of moderate interactions and 123 were of major interactions. Majority of the major interactions (208) were observed in the age group 61-80 years. Ofloxacin + Ondansetron and Metformin + Ofloxacin were found to be the most common interacting pairs in this study. The authors concluded that prevalence of drug-drug interactions can be more in ICU patients due to the polypharmacy. To improve the quality of life of the patients, rationale combination should be prescribed by the physicians along with the pharmaceutical care provided by the pharmacist.[27]

6. Mandana Moradi Dirin et al., (2014) conducted a prospective study to “evaluate and compare type and prevalence of drug-drug interactions in prescriptions dispensed in both community and hospital setting in Zabol, Iran”. From community and hospital settings, a total of 2796 prescriptions were collected and were processed for the detection of drug-drug interactions by using Lexi-comp drug interaction software. At least one potential DDI was observed in 41.6% of the prescriptions. According to Lexi-comp drug interaction software, the identified DDIs can be categorized into A, B, C, D & X and in this study, most of the interactions were of type C (66%). The most common drug combinations observed in this study were observed to be Fluvoxamine + Thioridazone, Imipramine + Thioridazone, Erythromycin + Cisapride and Azithromycin + Thioridazone. When compared to the hospital pharmacies, the percentage of drug interactions in community pharmacies were significantly lower. The authors finally concluded that, physicians must
be properly educated regarding the potential DDIs and the pharmacists should actively participate in the identification and prevention of drug related injuries that could prevent the consequence of DDIs among the patients\[33\].

7. **Rhanna Emanuela Fontenele Lima de Carvalho et al., (2013)** conducted a retrospective study to determine the “prevalence of drug interactions in intensive care units (ICUs) and to analyze the clinical significance of the identified interactions”. This study was conducted in seven intensive care units of teaching hospitals in Brazil among 1124 patients. From the prescriptions, details of the drugs administered at 24 hours and 120 hours of hospitalization were collected and analyzed by using “Drug Reax”. About 70.6% of the patients had at least one drug interaction within 24 hours. The number of interactions at 24 hours was found to be 2299 and at 120 hours it was found to be 2619. Majority of the interactions were of moderate severity (50.1%). Fentanyl + Midazolam and Captopril + potassium chloride were observed to be the most common interacting pairs observed in this study\[53\].

8. **Mohammad Ismail et al., (2013)** conducted a retrospective study to identify the “frequency, levels and predictors of potential drug-drug interactions in pediatric ward of a teaching hospital in Pakistan”. By using Micromedex Drug-Reax software, drug profiles of 400 pediatric patients were evaluated for potential drug-drug interactions. In this study, a total of 260 potential drug-drug interactions were detected in which 86 interacting drug combinations were involved. Regardless of severity type, 25.8% of the patients were exposed to at least one potential drug-drug interaction and 10.7% of the patients were exposed to at least one major potential DDI, 15.2% were exposed to at least one moderate potential DDI and 12.5% were exposed to at least one minor potential DDI. Majority of the interactions were of moderate severity (41.5%) followed by minor (35.4%) and major (21.9%). Finally, the authors concluded that moderate interactions were found to be more and patients with increased number of prescribed drugs were mostly exposed to drug-drug interactions\[54\].
9. **Sarah Mahmoud Abd El Samia Mohamed (2013)**, conducted a prospective study on the “prevalence and pattern of potential drug-drug interactions in the critical care units”. In this study, 750 patients were included whose prescriptions contain $\geq 4$ drugs. Drug interaction checker software “Drug Interaction Facts”, Stockley’s drug interactions and British National Formulary (BNF) along with online free drug interaction checker programs were used to analyze the prescription for drug-drug interactions. About 53.07% was found to be the prevalence of potential DDIs among the critical care unit (CCU) patients and 2.98±1.91 was observed to be the mean number of interactions occurred per patient. Majority of the interactions were of moderate severity (52.83%) followed by major (32.21%) and minor (14.96%). In this study, the prevalence of potential DDIs was significantly affected by age of the patient and the number of prescribed drugs \[^7\].

10. **Shahabudin Soherwardi et al., (2012)** conducted a prospective study on the “surveillance of the potential drug-drug interactions in the medicine department of a tertiary care hospital”. Analyzation was done by using Micromedex and other standard references for 250 cases and the prevalence in this study was found to be 66%. Drug-drug interactions were observed in patients who received drugs that ranged from 5-18. Majority of the interactions were occurred in patients who received cardiovascular drugs and most of the interactions were of moderate severity. In this study, the authors concluded that gender and age did not have a significant effect on the drug-drug interactions and most of the drug-drug interactions were preventable. The commonly occurred DDIs in this study were found to be in between fluoroquinolones & oral antidiabetics, Iron & Pantoprazole and Aspirin & Clopidogrel \[^4\].

11. **Hossein Rafiei et al., (2012)** conducted a study on the “prevalence of potential drug interactions in critical care units”. It was a retrospective study in which prescriptions of 371 patients admitted in the intensive care unit was studied. Drug Interaction Facts published in 2010 was used as a reference to
determine the drug interactions in this hospital. In the first 24 hours of prescription, about 726 cases were observed with drug interactions. Most of the interactions were of delayed, moderate and possible interactions. The most common drug combinations observed in this study was found to be Ranitidine + Phenytoin and Phenytoin + Dopamine. The authors found a significant correlation between the number of drug interactions and prescribed drugs, gender, age, duration of hospitalization and the number of prescribers. They concluded that medical team has to pay more attention towards the critical care unit patients because they usually possess more number of risk factors for the occurrence of drug interactions \[55\].

12. Adriano Max Moreira Reis et al., (2011) investigated the “prevalence of potential drug interactions at the intensive care unit of a university hospital in Brazil and analyzed their clinical significance”. About 299 patients were included who were admitted in the intensive care unit of the hospital in this retrospective cross sectional study. DRUG-REAX software was used to detect and analyze the potential drug-drug and drug-enteral nutrition interactions. The prevalence of the potential drug interactions was found to be 70%. The severity of the most of the interactions was found to be severe and moderate. The most common drug combinations observed in this study was found to be Fentanyl + Midazolam. The pharmacotherapy factors associated with potential drug interactions were drugs that induced Cytochrome P450 and drugs that prolong the QT interval. The authors concluded that due to the complexity of the pharmacotherapies administered, potential drug interactions were more prevalent in the intensive care unit and the interactions were associated with the number of drugs, characteristics of the administered drugs and as well as the length of the stay \[35\].

13. Fita Rahmawati et al., (2010) conducted a study to determine the “occurrence of potential drug-drug interactions and the association between the number of drugs and DDIs. This study was a retrospective observational study in which 100 geriatric inpatient cases were screened for drug-drug
interactions by using “Drug Interaction Facts” software. About 65% of the cases were observed with potential DDIs. The increase in the number of drugs used per day increased the number of potential DDIs. Geriatric patients consuming nine or more drugs found to have more DDIs (6.8±5.5). The number of drugs used per day has positive relationship on number of drug-drug interactions was indicated by linear regression analysis. The authors finally concluded that incidence of DDIs was frequent in geriatrics and pharmacists should play a crucial role in the management and prevention of DDIs [56].

14. Priska Vonbach et al., (2008) conducted a prospective study to assess the “potential drug-drug interactions at hospital admission, during hospitalization and at discharge and to evaluate the number of potential DDIs created during hospitalization in the internal medicine department”. By using the Pharmavista screening program, the drugs of 851 patients were screened for potential DDIs. The frequency of major and moderate potential DDIs per patient was observed to be 1.11 during hospitalization that was found to be greater when compared to hospital admission (0.59) or during discharge (0.60). At hospital admission, the frequency of major and moderate potential DDIs per drug prescribed or per drug pairs analyzed was higher when compared to hospital discharge. At discharge, majority of the major and moderate potential DDIs were due to a drug change during hospitalization. Potassium + Potassium sparing diuretic was the most common drug combination observed in this study. Finally, the authors concluded that to minimize the harm associated with DDIs, prescribing drugs with a low risk of potential DDIs along with careful monitoring of the adverse reactions [57].

15. Hui-Ling Liao et al., (2008) conducted a cross sectional study to assess the “prescribed drugs of nursing home residents, the occurrence of DDIs and the association between the number of drugs and DDIs in order to reinforce drug safety in the elderly patients”. Drug-Drug interactions database information system constructed by the department of health, Taiwan was used for the
analyzation of Drug-Drug interactions. A total of 323 patients were involved in the study and among them 81 (25.1%) had experienced DDIs. Majority of the interactions were of moderate severity (64.95%). As the number of drugs used per residents increased consequently the number of potential DDIs also increased. When compared to the prescriptions with one or two drugs, the prescriptions with nine or more drugs tended to have more number of DDIs. The authors finally concluded that the number of DDIs for the geriatrics with chronic diseases should be properly controlled in order to reduce the potential DDIs [58].