Adverse Drug Reactions and its Management Associated with Cancer Chemotherapy

Sanija P¹, Nandakumar U P¹, Jayaram Shetty K², Bharath Raj K C¹, Vinay B C¹, Sharad Chand¹, Juno J Joel*¹

¹Department of Pharmacy Practice, NGSM Institute of Pharmaceutical Sciences, Nitte (Deemed to be University), Paneer, Deralakatte, Mangaluru-575 018, Karnataka, India
²Department of Oncology, Justice K.S. Hegde Charitable Hospital, Nitte (Deemed to be University), Mangaluru-575 018, Karnataka, India

ABSTRACT

Adverse Drug Reactions (ADRs) are the problem that adds extra burden in the global scenario. Anticancer drugs can lead to severe negative consequences due to these ADRs. This study was conducted to assess the causality, severity and preventability of the identified ADRs of chemotherapeutic drugs among hospitalized patients diagnosed with cancer and also to analyze its management. A prospective observational study was conducted among cancer patients for a period of eight months. A total of 120 hospitalized patients who developed at least one ADR due to chemotherapy were included in this study. Data were collected and documented in a well-designed data collection form. A total of 166 ADRs were detected in 120 patients. Anaemia 33(19.8%), was found as the most commonly identified ADR. Patients administered with cisplatin as monotherapy were found to be reported with the highest number of ADRs (36). According to Naranjo’s scale and WHO causality assessment, 110(66.2%) and 105(63.2%) ADRs were found probable. Hartwig & Siegel scale of severity showed that 97(58.4%) ADRs were moderate and Modified Schumock and Thornton scale revealed that 129(77.7%) ADRs were not preventable. The patients prescribed with cisplatin, paclitaxel-carboplatin, epirubicin-oxaliplatin-capectabine regimen should be strictly and continuously monitored for the symptoms of ADR. Early detection of ADR can decrease morbidity and mortality.

INTRODUCTION

Cancer cells are abnormal cells that continuously divide indefinitely (Nandakumar and Joel, 2020). This condition is managed by using different treatment modalities such as radiotherapy, surgery and chemotherapy. Adverse drug reaction is regarded as a significant consequence of chemotherapeutic drugs; therefore, they cannot be prescribed in larger doses to treat cancer (Mrugank and Hareesha, 2013) and (Anusha et al., 2018). There is always a risk of adverse drug reactions associated with the intake of medicines (Rachana et al., 2019). These effects occur at normal dose, hence require careful monitoring of patients who are under long term therapy (Chand et al., 2009) and (Voora et al., 2019).
The World Health Organization defines ADR as “any response to a drug which is noxious and unintended, and which occurs at doses used in man for prophylaxis, diagnosis or treatment” (Shareef et al., 2018). ADRs contribute to overall health care costs by increasing morbidity and mortality in severe cases (Palaniappan et al., 2014).

The safety profile of cancer therapy still remains a question. ADR reporting programs done in hospitals may help in the determination of risks related to the drug and thereby enhances the effectiveness of therapy (Sharma et al., 2015) and (Voora et al., 2020). With this background, a study was conducted to find out the adverse drug reaction profile and its management, to analyze the characteristics of ADRs including the classes of drugs that most commonly cause ADRs and to assess the causality, severity and preventability of ADRs reported.

MATERIALS AND METHODS

A prospective observational study was conducted for the period of eight months in a tertiary care teaching hospital situated in Mangalore. Institutional Ethics Committee approval was obtained before initiating the study. In-patients of the oncology ward who were managed with chemotherapeutic drugs and who developed an ADR were enrolled in the study after obtaining their informed consent. Once an ADR is identified, it was confirmed with treating physicians and the assessment was made. Drugs used during the hospitalization, the reaction to the drug, management of ADR, outcome of therapy were documented in a suitably designed patient data collection form and ADR reporting form. The identified ADRs were subjected to causality assessment using the WHO-UMC causality assessment scale and Naranjo’s scale. The severity level was analyzed utilizing the Hartwig & Siegel scale and preventability by using Modified Shumock and Thornton scale. All the ADRs were reported in Suspected Adverse Drug Reporting Form, provided by the Indian Pharmacopoeia Commission (National Coordination Centre- Pharmacovigilance Programme of India). Data analysis was carried out using statistical package for social sciences (version 16.0).

RESULTS

Out of 120 in-patients who were diagnosed with cancer and who developed ADR due to chemotherapy, 82(68.3%) were males and 38(31.7%) were females. Most of the patients were in the age group of 50-59 years 41(34.2%), followed by 35(29.2%) patients of 40-49 years and 23(19.2%) of 60-69 years.

Majority of the patients were found diagnosed with carcinoma of breast 19(15.8%) followed by lung cancer 16(13.4%). The details are summarized in Table 1.

The anticancer drugs that were administered on the study population are presented in Table 2. Out of 120 patients, 29(24.1%) received monotherapy of cisplatin, a platinum analogue followed by combinations of paclitaxel + carboplatin (PC) 10(8.3%) and epirubicin+oxaliplatin+capecitabine (EOX) 9(7.4%).

A total of 166 ADRs were identified and gastrointestinal system, 52(31.3%) was found to be the most affected organ system with ADRs such as nausea, vomiting, mucositis, stomatitis, diarrhea, constipation, anorexia and abdominal pain followed by haematological abnormalities, 49(29.5%). The other organ systems affected were skin and appendages 18(10.8%), nervous system 6(3.6%), endocrine 3(1.8%), sensory organs 2(1.2%) and renal 1(0.6%). The most commonly observed ADR was anaemia 33(19.8%), followed by vomiting 11(6.6%) and pain on the limbs 11(6.6%). The complete details are referenced in Table 3.

In monotherapy, cisplatin was found to be the drug which caused more number of ADRs(36), followed by paclitaxel with 6 ADRs (Figure 1). Among combination therapy, paclitaxel + carboplatin was found to cause 20 ADRs followed by epirubicin+ oxaliplatin+capecitabine (10). The details are given in Table 4.

Figure 1: ADRs caused by drugs given as monotherapy

The number of ADRs per patient is summarized in Table 5. It was found that 84 patients were affected with one ADR out of which 57 were males and 27 were female patients. Twenty-eight patients were with two ADRs (18 males and 10 females), 6 patients with three ADRs (5 males and 1 female) and 2 male patients were with four ADRs.

The causality was assessed by using Naranjo’s and...
Table 1: Distribution pattern of cancer among the study population

| Sl. No | Types of Cancer | Frequency (n=120) | Percentage (%) |
|--------|-----------------|------------------|----------------|
| 1      | Breast          | 19               | 15.8           |
| 2      | Lung            | 16               | 13.4           |
| 3      | Stomach         | 15               | 12.5           |
| 4      | Buccal mucosa   | 11               | 9.2            |
| 5      | Lymphoma        | 10               | 8.3            |
| 6      | Liver           | 7                | 5.8            |
| 7      | Tongue          | 6                | 5.0            |
| 8      | Ovary           | 5                | 4.2            |
| 9      | Oesophagus      | 4                | 3.3            |
| 10     | Glottis         | 3                | 2.5            |
| 11     | Colon           | 3                | 2.5            |
| 12     | Bone            | 3                | 2.5            |
| 13     | Pancreas        | 3                | 2.5            |
| 14     | Maxilla         | 2                | 1.7            |
| 15     | Retromolartrigone | 2       | 1.7            |
| 16     | Neck            | 2                | 1.7            |
| 17     | Brain           | 2                | 1.7            |
| 18     | Nasopharyngeal  | 1                | 0.8            |
| 19     | Penis           | 1                | 0.8            |
| 20     | Foot            | 1                | 0.8            |
| 21     | Urinary tract   | 1                | 0.8            |
| 22     | Anal            | 1                | 0.8            |
| 23     | Oropharynx      | 1                | 0.8            |
| 24     | Skin            | 1                | 0.8            |

WHO-UMC causality assessment scales. According to Naranjo’s scale, 110 (66.2%) ADRs were probable, 43 (25.9%) were possible, 9 (5.4%) were definite and 4 (2.4%) were unlikely. WHO-UMC criteria showed that 105 (63.2%) ADRs were probable followed by 42 (25.3%) possible, 13 (7.8%) certain and 6 (3.6%) unlikely reactions. The severity of ADRs was assessed with the help of Hartwig & Siegal scale. This revealed that 97 (58.4%) ADRs were of moderate severity, 64 (38.5%) were mild and 5 (3.0%) were severe.

Preventability was assessed by using the Modified Shumock and Thornton preventability scale. According to this scale, 129 (77.7%) ADRs were not preventable, 35 (21.1%) were probably preventable and 2 (1.2%) were definitely preventable. ADRs were managed by using different methods. 120 (72.3%) ADRs were managed by providing additional treatment without changing the drug regimen. 39 (23.5%) were managed without any additional treatment and in case of 7 (4.2%) ADRs, chemotherapy were postponed to minimize the severity.

Specific treatment was given to treat 73 (44%) ADRs whereas symptomatic treatment was given for 51 (30.7%). 42 (25.3%) ADRs required no treatment. Out of 166 ADRs identified, 138 (83.1%) were found recovered, 19 (11.4%) were of not recovered or continuing status and 9 (5.4%) ADRs were found to have an unknown status. Various classes of drugs were used to treat the ADRs caused by chemotherapy regimen.

Before starting chemotherapy, parenteral dexamethasone, ranitidine and ondansetron were mostly administered as pre-medication. Filgrastim, blood transfusion, vitamin B12 and iron preparations were given for the management of haematological ADRs. Antiemetics such as ondansetron and domperidone were used in emesis.

Rifaximin and glycerol were given for diarrhoea whereas normal saline and parenteral preparation of potassium and calcium chloride for the electrolyte imbalance. Analgesics such as acetaminophen, mefenamic acid, diclofenac sodium and morphine were prescribed for pain management. Vitamin B complex and multivitamin tablets were used for the symptomatic relief of anorexia. Aluminum hydroxide, magnesium hydroxide, stomatab (astringent
Table 2: Pattern of chemotherapy regimen prescribed among patients

| Sl.No | Chemotherapy regimen                              | Frequency | Percentage (%) |
|-------|---------------------------------------------------|-----------|----------------|
| 1     | Cisplatin                                         | 29        | 24.1           |
| 2     | Paclitaxel+Carboplatin                            | 10        | 8.3            |
| 3     | Epirubicin+Oxaliplatin+Capecitabine               | 9         | 7.4            |
| 4     | Carboplatin+Docetaxel                             | 7         | 5.8            |
| 5     | Cyclophosphamide+Doxorubicin                      | 6         | 5.0            |
| 6     | Etoposide+Carboplatin                             | 5         | 4.1            |
| 7     | Capecitabine                                      | 4         | 3.3            |
| 8     | Gemcitabine+Oxaliplatin                           | 4         | 3.3            |
| 9     | Paclitaxel                                        | 3         | 2.5            |
| 10    | Epirubicin+Fluorouracil                           | 3         | 2.5            |
| 11    | Epirubicin+Fluorouracil+Cisplatin                 | 3         | 2.5            |
| 12    | Pemetrexed                                        | 3         | 2.5            |
| 13    | Carboplatin+Gemcitabine                           | 3         | 2.5            |
| 14    | Carboplatin                                       | 2         | 1.7            |
| 15    | Fluorouracil                                      | 2         | 1.7            |
| 16    | Rituximab+Doxorubicin+Vincristine                 | 2         | 1.7            |
| 17    | Bortezomib                                        | 2         | 1.7            |
| 18    | Etoposide+Cisplatin                               | 2         | 1.7            |
| 19    | Cyclophosphamide                                  | 2         | 1.7            |
| 20    | Dacarbazine                                       | 2         | 1.7            |
| 21    | Docetaxel                                         | 1         | 0.8            |
| 22    | Gemcitabine                                       | 1         | 0.8            |
| 23    | Rituximab                                         | 1         | 0.8            |
| 24    | Cetuximab+Paclitaxel                              | 1         | 0.8            |
| 25    | Cetuximab+Methotrexate                            | 1         | 0.8            |
| 26    | Doxorubicine+Docetaxel                            | 1         | 0.8            |
| 27    | Trastuzumab+Cyclophosphamide+Doxorubicin          | 1         | 0.8            |
| 28    | Bendamustine                                      | 1         | 0.8            |
| 29    | Oxaliplatin                                       | 1         | 0.8            |
| 30    | Bortezomib+Cyclophosphamide                       | 1         | 0.8            |
| 31    | Epirubicin+Capecitabine                           | 1         | 0.8            |
| 32    | Gemcitabine+Cisplatin                             | 1         | 0.8            |
| 33    | Epirubicin+Fluorouracil+ Cyclophosphomide         | 1         | 0.8            |
| 34    | Vincristine                                       | 1         | 0.8            |
| 35    | Rituximab+Gemcitabine+Oxaliplatin                 | 1         | 0.8            |
| 36    | Epirubicin                                        | 1         | 0.8            |

DISCUSSION

The narrow therapeutic index of cancer treatments makes the pharmacovigilance studies necessary in oncology. A proper ADR-reporting programme may be useful in minimizing the ADRs, and to provide better patient care. In this study, out of 120 patients who were diagnosed with cancer and developed ADR due to chemotherapy, 82(68.3%) were males and 38(31.7%) were females. The occurrence of cancer was more in the age group of 50-59 years (34.2%) and was comparable with the study done by Goyal et al. (2014). Whereas in the study carried out by Thapaliya et al. (2015) in Nepal, the prevalence of cancer was more in the age group of 30-45. The most common diagnosis made among the patients enrolled for the study was breast carcinoma...
Table 3: ADRs and Organ system affected

| Organ system affected | ADR               | Frequency | Percentage (%) |
|-----------------------|-------------------|-----------|----------------|
| Nervous               | Neuropathy        | 10        | 6.0            |
|                       | Headache          | 1         | 0.6            |
|                       | Seizure           | 1         | 0.6            |
| GI                    | Nausea            | 10        | 6.0            |
|                       | Vomiting          | 11        | 6.6            |
|                       | Mucositis         | 8         | 4.8            |
|                       | Stomatitis        | 3         | 1.8            |
|                       | Diarrhea          | 5         | 3.0            |
|                       | Constipation      | 4         | 2.4            |
|                       | Abdominal pain    | 9         | 5.4            |
|                       | Anorexia          | 2         | 1.2            |
| Hematology            | Anaemia           | 33        | 19.8           |
|                       | Leucopenia        | 6         | 3.6            |
|                       | Thrombocytopenia  | 6         | 3.6            |
|                       | Febrile neutropenia| 2     | 1.2            |
|                       | Neutropenia       | 2         | 1.2            |
| Skin and appendages   | Alopecia          | 8         | 4.8            |
|                       | Nail discoloration| 4         | 2.4            |
|                       | Itching           | 6         | 3.6            |
| Musculoskeletal       | Pain on injection site| 1    | 0.6            |
|                       | Pain on the limbs | 11        | 6.6            |
| Respiratory           | Dyspnea           | 3         | 1.8            |
|                       | Cough             | 3         | 1.8            |
| Endocrine             | Hyponatremia      | 2         | 1.2            |
|                       | Hypocalcemia      | 1         | 0.6            |
| Renal                 | Abnormal blood urea| 1      | 0.6            |
| Sensory organs        | Visual disturbances| 1       | 0.6            |
|                       | Hearing disturbances| 1    | 0.6            |
| Others                | Fatigue           | 8         | 4.8            |
|                       | Fever             | 2         | 1.2            |

ADRs: adverse drug reactions

19(15.8%) followed by lung, 16(13.4%). But in a study done by Sisay et al. (2015) the most common diagnosis made was gastrointestinal cancer (29.4%) followed by head and neck cancer (18.8%). These results were found comparable with the study conducted by Goyal et al. (2014) in which the predominant types were lung cancer (22.86%) and breast cancer (18.1%).

A total of 166 ADRs were identified among 120 patients who received chemotherapy. Among them, 82 male patients were identified with 116 (69.9%) ADRs and 38 female patients with 50 (30.1%) ADRs. This finding was consistent with the study done by Prasad et al. (2013). However in some other studies conducted by Sharma et al. (2015) and Poddar et al. (2009), female predominance was seen and this difference could be attributed to the hormonal changes occurring in females during different stages of their life. Cisplatin (24.1%), followed by a combination of paclitaxel with carboplatin (8.3%) were the most commonly prescribed chemotherapeutic agents. Out of the individual drugs given, cisplatin caused more number of ADRs, 36. Among drug combinations, paclitaxel-carboplatin combination (20) was found to cause the maximum number of ADRs. These results were similar to the study done by Khandelwal et al. (2015). The most commonly affected organ system by chemotherapy-induced ADR was the gastrointestinal system, 52(31.3%) and the result was found comparable with the study conducted by Thapaliya et al. (2015). But it was in contradiction with the study carried out in South India by Khandelwal et al. (2015). Since it has shown
Table 4: ADRs caused by drugs given in combination

| Sl. No | Drug Combinations                  | Frequency of ADRs |
|-------|------------------------------------|-------------------|
| 1.    | Paclitaxel+Carboplatin             | 20                |
| 2.    | Epirubicin+Oxaliplatin+Capecitabine | 10                |
| 3.    | Cyclophosphamide+Doxorubicin       | 8                 |
| 4.    | Epirubicin+Fluorouracil+Cisplatin  | 7                 |
| 5.    | Carboplatin+Docetaxel              | 7                 |
| 6.    | Gemcitabine+Oxaliplatin            | 5                 |
| 7.    | Etoposide+Carboplatin              | 5                 |
| 8.    | Epirubicin+Fluorouracil            | 4                 |
| 9.    | Rituximab+Gemcitabine+Oxaliplatin  | 3                 |
| 10.   | Gemcitabine+Cisplatin              | 3                 |
| 11.   | Etoposide+Cisplatin                | 3                 |
| 12.   | Carboplatin+Gemcitabine            | 3                 |
| 13.   | Trastuzumab+Cyclophosphamide+Doxorubicin | 2          |
| 14.   | Rituximab+Doxorubicin+Vincristine  | 2                 |
| 15.   | Cetuximab+Paclitaxel               | 2                 |
| 16.   | Cetuximab+Methotrexate             | 2                 |
| 17.   | Bortezomib+Cyclophosphamide        | 2                 |
| 18.   | Epirubicin+Fluorouracil+ Cyclophosphamide | 1          |
| 19.   | Epirubicin+ Capecitabine           | 1                 |
| 20.   | Doxorubicine+ Docetaxel            | 1                 |

ADRs: adverse drug reactions

Table 5: Distribution of patients according to number of ADRs identified

| No of ADRs | Male Frequency | Female Frequency | Total |
|------------|----------------|-----------------|-------|
| 1          | 57             | 27              | 84    |
| 2          | 18             | 10              | 28    |
| 3          | 5              | 1               | 6     |
| 4          | 2              | 0               | 2     |
| Total      | 82             | 38              | 120   |

hematological system as the most affected one. The commonest adverse drug reaction was anaemia 33 (19.8%) followed by pain in upper and lower limbs and vomiting, 11(6.6%) each. Only few studies have reported anaemia as the most frequently observed ADR (Khandelwal et al., 2015). A study carried out by Sharma et al. (2015) reported infections (22.4%) as the most common ADR. Chemotherapy regimens are more toxic to rapidly dividing cells such as bone marrow cells, which can lead to myelosuppression and affect blood cells. Platinum compounds including cisplatin and carboplatin prominently causes vomiting because of the direct stimulation of chemoreceptor trigger zone.

According to the Naranjo Scale, 66.2% of ADRs were probable and 25.9% were possible in terms of causality. (Prasad et al., 2013) conducted a study on ADRs in a hospital of Kolkata and reported that 62.22% of ADRs were probable and 31.11% were possible which was found similar to our report. According to the WHO-UMC causality assessment scale, 63.2% of ADRs were probable and 25.3% were possible. Similarly, in study done by Poddar et al. (2009), probable ADRs were more commonly identified followed by possible ADRs, whereas in the study by Mistry et al. (2015), 72% of ADRs were possible and 15% of ADRs were unlikely. In the present study, moderately severe ADRs were found to be 58.4% of the total reactions and 38.5% were mild. ADRs such as leucopenia, thrombocytopenia, which constituted 3% of the total reactions, were found to be severe. Similar result was obtained in a study done by Mistry et al. (2015) where 67.05% were moderate and 28.96% were mild reactions. Out of
166 ADRs, 77.7% were not preventable, 21.1% were probably preventable. This report is consistent with the result obtained by Khandelwal et al. (2015) where, 80.75% of ADRs were not preventable. Management of 72.3% of ADRs was done by giving additional treatment without changing the chemotherapy regimen and 23.5% ADRs were managed without any additional treatment. 83.1% of ADRs were found to be recovered and 11.4% did not recover during the study period. A study done by Khandelwal et al. (2015) also concluded that the ADRs reported were managed with additional treatment and most of them were found recovered.

CONCLUSION

Patient safety is fetching a global concern nowadays. The primary obligation of this is to control ADRs. Early detection and monitoring of ADR may help in reducing the health hazards. In the present study, the common type of cancer observed was breast cancer. The occurrence of carcinoma was found to be predominant in males. The study showed that most of the ADRs were caused by agents of individual chemotherapy regimen such as cisplatin and combinations like paclitaxel-carboplatin(PC) and epirubicin-oxaliplatin-capetabine(EOX). Patients receiving these regimens should be rigorously and constantly monitored for the symptoms of ADR. The causal relationship of most of the ADRs identified was probable, according to Naranjo and WHO-UMC scales. Most of them were moderately severe and were not preventable. Clinical pharmacists can play a pivotal role by joining with the health care team to decrease the occurrence of ADRs by early detection and prevention and can also help in the management of suspected ADRs.

ACKNOWLEDGEMENT

We would like to extend our sincere gratitude towards the staff of Department of Pharmacy Practice and to all doctors, nurses, and paramedical staff of Justice K.S. Hegde Charitable Hospital for their kindness and co-operation during various stages of this research work.

Funding Support

The authors declare that they have no funding support for this study

Conflict of Interest

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

REFERENCES

Anusha, R., Chand, S., Lal, V., Sushmitha, D. M., Reddy, D. S., Tejaswini, S., Chitrahasini, S. 2018. Isoniazid Induced Liver Injury; a Case Series and Review. Journal of Pharmacy Practice and Community Medicine, 4(2):128–130.

Chand, S., Bhandari, R., Girish, H. N., Sukeerthi, D., Sah, S. K., Voora, L. 2009. Isoniazid Induced Psychosis. Journal of Global Pharma Technology, 11(05):11–14.

Goyal, Y. N., Solanki, K. C., Mistry, R. A., Joshi, N. D., Singh, A. P., Gajera, M. V. 2014. Pattern of adverse drug reactions due to cancer chemotherapy in tertiary care teaching hospital in Gujarat. Int J Sci Res, 3(1):333–335.

Khandelwal, S., Bairiy, K. L., Vidyasagar, M. S., Chogtu, B., Sharan, K. 2015. Adverse drug reaction profile of cancer patients on chemotherapy in a tertiary care hospital. International Journal of Pharma and Bio Sciences, 6(2):233–244.

Mistry, C. B., Rama, D. S., Batra, V. D. 2015. Study of impact of adverse drug reaction of chemotherapy on treatment outcome, overall morbidity and mortality of oral cavity squamous cell carcinoma. Int. Res. J. Medical Sci, 3(7):13–23.

Mrugank, B. P., Hareesha, R. P. 2013. Prospective observational, non-randomized, parallel sequence study for assessment of adverse drug reactions due to chemotherapeutic treatment in different types of cancer patients. International Journal of Pharmaceutical Sciences and Research, 4(1):386–391.

Nandakumar, U. P., Joel, J. J. 2020. Oncopharmacists: The Game Changers in Cancer Therapy. Journal of Young Pharmacists, 12(1):15–17.

Palaniappan, M., Srinivasamurthy, S. K., Dubashi, B. 2014. Neurological adverse drug reactions of anti-cancer drugs. IJRPP, 3(3):152–157.

Poddar, S., Sultana, R., Sultana, R., Akbor, M. M., Azad, M. A. K., Hasnat, A. 2009. Pattern of adverse drug reactions due to cancer chemotherapy in tertiary care teaching hospital in Bangladesh. Dhaka University Journal of Pharmaceutical Sciences, 8(1):11–16.

Prasad, A., Datta, P. P., Bhattacharya, J., Pattanayak, C., Chauhan, A. S., Panda, P. 2013. Pattern of adverse drug reactions due to cancer chemotherapy in a tertiary care teaching hospital in Eastern India. J Pharmacovigilance, 1(2):107–107.

Rachana, J., Shastry, C. S., Mateti, U. V. 2019. Incidence and associated factors of adverse drug reactions in general medicine department of a tertiary...
care teaching hospital. *International Journal of Pharmaceutical Research*, 11(3):177–184.

Shareef, J., Nandakumar, U. P., Bhat, M. 2018. A study on assessment of adverse drug reactions in patients with Tuberculosis in a tertiary care teaching hospital. *J Appl Pharm Sci*, 8(4):99–104.

Sharma, A., Thomas, J., Bairy, K. L., Kumari, K., Manohar, H. 2015. Pattern of adverse drug reactions due to cancer chemotherapy in a tertiary care hospital in South India. *Perspectives in Clinical Research*, 6(2):109–115.

Sisay, E. A., Engidawork, E., Yesuf, T. A., Ketema, E. B. 2015. Drug related problems in chemotherapy of cancer patients. *J Cancer Sci Ther*, 7(2):55–59.

Thapaliya, K., Shrestha, A., Prajapti, A., Subedi, R., Giri, S. 2015. Study of pattern of adverse drug reaction due to cancer chemotherapy and their management in hospitalized patient in B P koirala Memorial Cancer Hospital. *Journal of Chitwan Medical College*, 4(4):24–28.

Voora, L., Sah, S. K., Bhandari, R., Shastry, C. S., Chand, S., Rawal, K. B., Vinay, B. C. 2020. Doctor of pharmacy: Boon for health-care system. *Drug Invention Today*, 14(1):153–158.

Voora, L., Shastry, S. C., Bhandari, R., Sukeerthi, D., Rawal, K. B., Chand, S. 2019. Phenytoin-Induced Erythroderma. *Journal of Young Pharmacists*, 11(3):320–321.