



Received on 17 March, 2016; received in revised form, 04 May, 2016; accepted, 31 May, 2016; published 01 August, 2016

## PREDICTION OF CHEMOTHERAPY PRESCRIBING ERRORS FOR ONCOLOGY PATIENTS

H. E. Barakat <sup>\*1</sup>, N. A. Sabri <sup>2</sup> and A. S. Saad <sup>3</sup>

Department of Clinical Pharmacy<sup>1</sup>, Faculty of Pharmacy, Ain Shams University, Cairo, Egypt.

Head of Clinical Pharmacy Department <sup>2</sup>, Faculty of Pharmacy, Ain Shams University, Cairo, Egypt.

Department of Clinical Oncology <sup>3</sup>, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

### Keywords:

Antineoplastic drugs, Prescribing errors, Risk factors, Prediction

### Correspondence to Author:

**H. E. Barakat**

The Faculty of Pharmacy,  
Ain Shams University, AL, Al  
Khalifa Al Mamoun St., Abbasia,  
Cairo, Egypt.

**E-mail:** haderehab7785@yahoo.com

**ABSTRACT:** The chemotherapy prescribing errors (PEs) can lead to tragic consequences for the oncology patients. This cross-sectional observational study aims to predict the incidence of prescribing errors involving chemotherapeutic agents, and review their severity, through examining a random sample of 500 cancer patients at the out-patient chemotherapy unit of Ain Shams University Hospital, Cairo, Egypt; from March 2014 till August 2014. British Columbia Cancer Agency (BCCA) data base was used as a reference to identify the PEs. Prescription errors were classified according to their incidence and severity; in addition the relation between the risk factors and the observed PEs was studied. The study revealed that all the cases contained at least one error, the most common error incidence was the unspecified tumor staging in the protocol template (n=341, 68%), followed by dose error incidence (n=317, 66%). The risk factors predicting the prescribing medication errors were identified as: the protocol type, the tumor type, the toxicity type of the antineoplastic regimen, and others. Therefore identification of risk factors leading to prescribing errors should be targeted for the prevention of these errors, as well as, improvement of treatment (TTT) plan of the oncology patients.

**INTRODUCTION:** A medication error (ME) is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer <sup>1</sup>. In a study of Medication errors in the Middle East countries it was found that 46% of the MEs occurred during the prescribing stage <sup>2</sup>. Prescription errors occurred during chemotherapeutic agent treatment can lead to tragic toxicities because of higher vulnerability of patients, complex treatment regimens, intensive combinations, and narrow therapeutic index of drugs.

When considering Medication errors, antineoplastic drugs are the second most common cause of death <sup>3</sup>, therefore numerous recommendations have been published in order to decrease the risk of errors <sup>4-6</sup>.

Prescription errors can vary in severity from minor to major faults such as inappropriate medication prescriptions, dose errors of the antineoplastic (Overdose related Incidents <sup>7-10</sup> could result in permanent damage or patient fatality <sup>11-14</sup>, while under doses could compromise the success of therapy), and drug-drug interactions, those errors could occur due to wrong judgment or lack of expertized prescriber <sup>15, 16</sup>.

Expanding clinical pharmacist professional roles can lead to the early identification of errors and their rectification before reaching the patients, to increase the success probability of the treatment plan. Therefore developing effective ways to

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| <p><b>QUICK RESPONSE CODE</b></p>                           | <p><b>DOI:</b><br/>10.13040/IJPSR.0975-8232.7(8).3274-83</p> |
| <p>Article can be accessed online on:<br/><a href="http://www.ijpsr.com">www.ijpsr.com</a></p>   |  |
| <p>DOI link: <a href="http://dx.doi.org/10.13040/IJPSR.0975-8232.7(8).3274-83">http://dx.doi.org/10.13040/IJPSR.0975-8232.7(8).3274-83</a></p> |  |

reduce errors requires the identification of their causes, in addition to the factors associated with the error incidence<sup>17</sup>. Several studies have addressed prescribing errors in the oncology service. On the contrary few studies have evaluated the effect of studying factors leading to chemotherapy-related prescribing errors.

In a cross-sectional study at an Adult Oncology Clinic in a main hospital in Alexandria, Egypt; showed that the proportion of errors in chemotherapy medication orders and hence the intervention rate was 66.6%<sup>18</sup>, another study conducted in a tertiary care teaching hospital in South India found that a total of 4253 prescribing errors occurred in 1500 prescriptions (283.5%), of which 47.1% were due to omissions like name, age and diagnosis, in which the potentially harmful errors that were likely to result in serious consequences to the patient were estimated to be 11.7%<sup>19</sup>. Another 2 year observational study aimed to identify the predictors of medication prescribing errors involving anticancer treatments, risk factors identified as predictors of oncology related errors were patients with body surface area >2 m<sup>2</sup>, protocols involving more than three antineoplastic drugs, and inpatient care<sup>17</sup>.

Our study aimed to identify the incidence and severity of PEs, as well as identifying predictors of prescribing errors in the oncology department

involving tumor-related, and anticancer related factors.

## MATERIALS AND METHODS:

### Study Design:

It is a cross-sectional observational study examining a random sample of out-patients, with proven malignant disease receiving chemotherapy, over a period of 6 months on a biweekly selection basis from March 2014 till August 2014 who visit the chemotherapy unit, Oncology department, Ain Shams University Teaching Hospitals. In which a number of 500 patients were observed during the whole study.

The patients were diagnosed in the oncology department specialized clinics, and then the patients were referred to the central chemotherapy unit to receive their decided chemotherapy regimen according to pre-printed custom-made protocol templates of different chemotherapy regimens. All study patients received their chemotherapy dose in the central chemotherapy clinic(CCC).

### 1- Identification and assessment of prescribing errors incidence, and severity:

Prescription errors have been defined as MEs initiated during the prescribing process. These prescribing errors were defined, as described in the **Table 1**.

**TABLE 1: CLASSIFICATION AND DEFINITION OF MEDICATION PRESCRIBING ERRORS.**

| Prescribing error   | Definition  |
|---|---|
| Unidentified protocol   | The protocol wasn't identified on BCCA database.  |
| Inappropriate medications                                       | Medication ordered was not appropriate for patient based on indication, patient-specific variables, or clinical status.   |
| Medication omission   | Patient having an indication for which no treatment or inadequate treatment was prescribed.                               |
| BSA calculation error   | BSA calculated by DuBois & DuBois equation differs from that calculated by physicians by more than +/- 5%.                |
| Dose error  | Under or overdose of more than 5% of antineoplastic drugs <sup>17</sup> .   |
| Dose omission   | Unspecified dosage for the medications.   |
| Wrong dose time   | The dose wasn't taken on the right day either it was delayed, or taken on time when it should be delayed.                 |
| Potential drug-drug interactions                                | Pharmacokinetic and pharmacodynamics interactions.  |
| Lab test omission   | Lab test specified for the protocol wasn't done before receiving the antineoplastic cycle.                                |
| Duplicate prescribing   | Two or more drugs from the same class are prescribed to treat the same condition, or different conditions <sup>23</sup> . |
| Omitted or improper route of administration of the chemotherapy | Unspecified route, wrong route, or improper route to the patient clinical status, and the protocol of choice.             |
| Wrong infusion volume and rate of the diluent                   | Wrong infusion rate or volume of the diluent for medications administrated via intravenous route.                         |

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|--|--|
| Improper follow up plan  | Improper or omitted physical examinations and other medical tests after a specified number of cycles to audit the enhancement of the case after receiving certain protocol so that we can take decisions by continuing, stopping , or shifting the protocol. |
| Illegible hand writing   | A crucial data in the prescription wasn't clear enough to be read.   |
| Protocol not signed  | The physician signature wasn't written on the protocol.  |
| Stage not specified  | Stage wasn't written by the physician.   |
| Missed patient number  | The serial ID number of the patient wasn't written.  |
| The intention of treatment was not complying with the protocol of choice | The protocol of choice isn't tailored to the intention of treatment for a specific patient.  |

In addition to relying on the professional clinical pharmacy knowledge, the following resources including online database were used to identify potential prescribing errors incidence: in which the prescriptions were analyzed using globalrph.com data base.<sup>20</sup>, to detect errors in BSA calculations, in addition to BC cancer agency (BCCA) cancer drug manual<sup>21</sup>, to identify errors including unidentified protocols, inappropriate medications, dose errors, improper diluent type and volume, as well as improper infusion rate, wrong follow up plan ,and non-compliance of intention of TTT to the protocol of choice. Drugs.com data base<sup>22</sup> was used to detect drug-drug interactions. The references used weren't the only right source, but they were chosen for their availability as open sources. The prescribing errors were classified according to their severity into 3 levels major, moderate, and minor<sup>23</sup>. In which, major means an adverse effect can cause permanent damage or life risk, moderate means an adverse effect can make harm and treatment is required, minor means small or no clinical effect, with no treatment required.

## 2-Identification and assessment of risk factors:

A risk factor is any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury<sup>24</sup>. So we studied the impact of risk factors on prescribing errors because they can play central part in the prediction and prevention of prescribing errors<sup>25</sup>. Two types of potential risk factors were identified in this study:

### a) Tumor related factors:

Tumor type (breast, lung, GIT, genitourinary, lymphoma, gynecology and others including head and neck cancer, melanoma, sarcoma, they were gathered in one category because of very few cases in each), as well as staging of tumor (early,

locally advanced, metastatic), the definition of each stage according to the National Cancer Institute, cancer staging fact sheet is as follows;

- **Early** means: cancer is limited to the organ in which it began, without evidence of spread.
- **Locally advanced** means: Cancer has spread beyond the primary site to nearby lymph nodes or organs and tissues.
- **Metastatic** means: Cancer has spread from the primary site to distant organs or distant lymph nodes.

### b) Chemotherapy related factors:

Intention of treatment (adjuvant, metastatic, palliative, neoadjuvant) protocol type(CHOP, Docetaxel protocols, FEC-100, FOLFOX, Gemcitabine protocols, Paclitaxel protocols, Trastuzumab, Zoledronic acid, and others), route of administration of chemotherapy(IV, PO), dose frequency( q21 d,q28 d), toxicity type of the chemotherapy cycle (Hematological, non-hematological, both, none or missed), number of cycles required (continuous variable data ), course number in the cycle (continuous variable data) , and total number of drugs received by the patient including antineoplastic agents, pre and post medications (continuous variable data).

## 3-The statistical analysis:

Summary statistics of the data was performed to determine the incidence of prescribing errors in the oncology department of Ain shams university hospitals, as well as their severity. The prediction of PEs was performed in two steps. Firstly, univariate analysis was performed to assess the relationship between potential risk factors and

observed medication errors; the level of significance was ( $p \leq 0.05$ ). Second, all borderline significant in univariate analysis were integrated into stepwise logistic regression model. The odds ratio (OR) and 95% confidence interval (CI) were computed.

**RESULTS:**

**Data collection:**

Between March 2014 and August 2014, a number of 500 chemotherapy receiving patients who

suffered solid tumors were studied. Including the risk factors under study, the missed data was excluded from the study. **Fig.1** shows the demographics of the patients under study.

Whereas the number of cycles required for the protocol of choice, course number in the cycle, and the number of medications in the treatment regimen (including antineoplastic drugs, pre- and post-medications) were studied as continuous variables and not categorized.

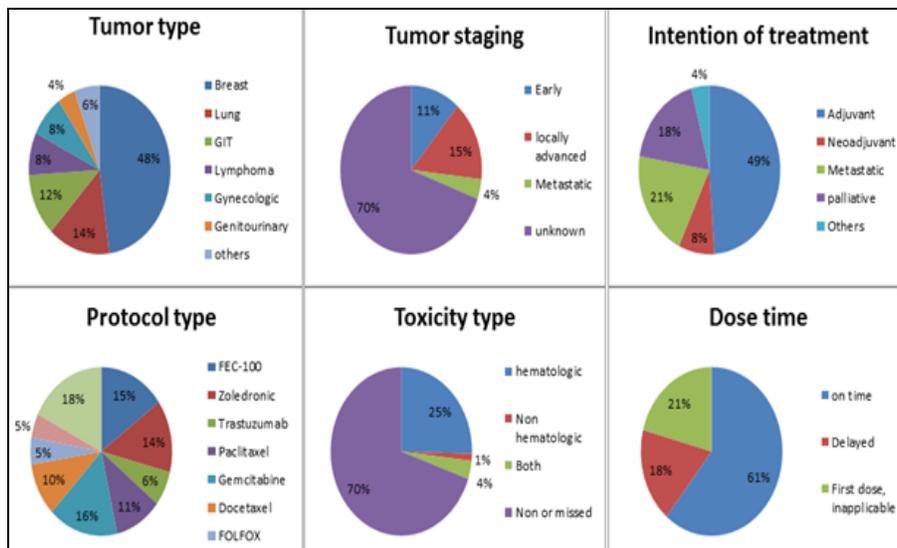


FIG.1: SHOWS THE DEMOGRAPHICS OF THE PATIENTS AND THEIR PERCENTAGE

**Prescriptions of antineoplastic:**

Among the 500 antineoplastic prescriptions 500 contained at least one prescription error (100%).

**Fig.2** shows the percentage of each error incidence, and severity.

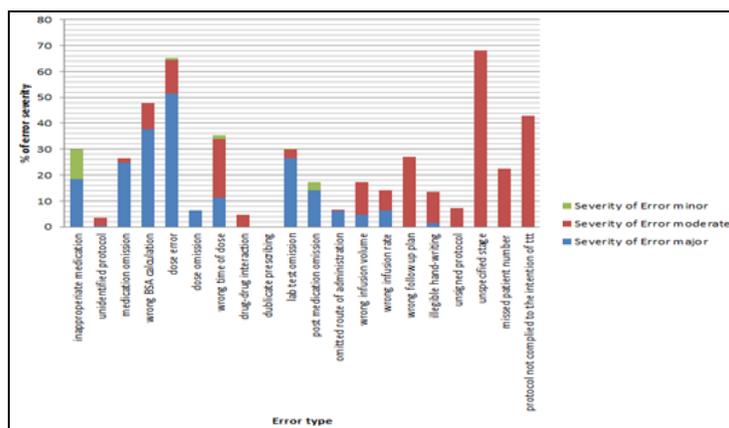


FIG.2: THE PERCENTAGE OF PRESCRIPTION ERROR INCIDENCE, AND SEVERITY

**Univariate analysis:**

Logistic regression model was applied for the categorical data; the data containing continuous values was analyzed using Mann-Whitney test as the distribution of data wasn't normally distributed.

The significant risk factors for the errors on the univariate level are summarized in the following tables.

**TABLE 2: UNIVARIATE ANALYSIS OF THE SIGNIFICANT RISK FACTORS FOR INAPPROPRIATE MEDICATION ERROR.**

| Risk factor   |                       | Inappropriate medication error |       |     |       | P-value |
|---------------|-----------------------|--------------------------------|-------|-----|-------|---------|
|               |                       | Non                            |       | Yes |       |         |
|               |                       | N                              | %     | N   | %     |         |
| Tumor type    | Breast                | 157                            | 65.7% | 82  | 34.3% | 0.035   |
|               | Genitourinary         | 18                             | 90.0% | 2   | 10.0% |         |
|               | GIT                   | 38                             | 63.3% | 22  | 36.7% |         |
|               | Gynecological         | 33                             | 82.5% | 7   | 17.5% |         |
|               | Lung                  | 49                             | 69.0% | 22  | 31.0% |         |
|               | Lymphoma              | 34                             | 82.9% | 7   | 17.1% |         |
| Protocol type | Others                | 21                             | 72.4% | 8   | 27.6% | <0.001  |
|               | CHOP                  | 22                             | 95.7% | 1   | 4.3%  |         |
|               | Docetaxel protocols   | 35                             | 68.6% | 16  | 31.4% |         |
|               | FEC-100               | 36                             | 48.0% | 39  | 52.0% |         |
|               | FOLFOX                | 17                             | 65.4% | 9   | 34.6% |         |
|               | Gemcitabine protocols | 60                             | 75.9% | 19  | 24.1% |         |
|               | Other                 | 61                             | 69.3% | 27  | 30.7% |         |
|               | Paclitaxel protocols  | 32                             | 59.3% | 22  | 40.7% |         |
|               | Trastuzumab           | 20                             | 60.6% | 13  | 39.4% |         |
|               | Zoledronic acid       | 65                             | 94.2% | 4   | 5.8%  |         |

**TABLE 3: UNIVARIATE ANALYSIS OF THE SIGNIFICANT RISK FACTORS FOR UNSPECIFIED STAGE ERROR**

| Risk factor     |                       | Unspecified stage error |       |       |       | P-value |
|-----------------|-----------------------|-------------------------|-------|-------|-------|---------|
|                 |                       | Non                     |       | Yes   |       |         |
|                 |                       | N                       | %     | N     | %     |         |
| Protocol type   | CHOP                  | 6                       | 26.1% | 17    | 73.9% | <0.001  |
|                 | Docetaxel protocols   | 18                      | 35.3% | 33    | 64.7% |         |
|                 | FEC-100               | 45                      | 60.0% | 30    | 40.0% |         |
|                 | FOLFOX                | 13                      | 50.0% | 13    | 50.0% |         |
|                 | Gemcitabine Protocols | 9                       | 11.4% | 70    | 88.6% |         |
|                 | Other                 | 30                      | 34.1% | 58    | 65.9% |         |
|                 | Paclitaxel protocols  | 15                      | 27.8% | 39    | 72.2% |         |
|                 | Trastuzumab           | 15                      | 45.5% | 18    | 54.5% |         |
| Zoledronic acid | 8                     | 11.6%                   | 61    | 88.4% |       |         |

**TABLE 4: UNIVARIATE ANALYSIS OF THE SIGNIFICANT RISK FACTORS FOR WRONG INFUSION VOLUME ERROR**

| Risk factor |          | Wrong infusion volume error |       |     |       | P-value |
|-------------|----------|-----------------------------|-------|-----|-------|---------|
|             |          | Non                         |       | Yes |       |         |
|             |          | N                           | %     | N   | %     |         |
| Tumor type  | Breast   | 194                         | 91.1% | 19  | 8.9%  | <0.001  |
|             | GIT      | 90                          | 89.1% | 11  | 10.9% |         |
|             | Lymphoma | 11                          | 47.8% | 12  | 52.2% |         |
|             | Other    | 118                         | 84.3% | 22  | 15.7% |         |

**TABLE 5: UNIVARIATE ANALYSIS OF THE SIGNIFICANT RISK FACTORS FOR IMPROPER MEDICATION INFUSION RATE ERROR.**

| Risk factor |          | Improper medication infusion rate error |       |     |       | P-value |
|-------------|----------|---|-------|-----|-------|---------|
|             |          | Non                                     |       | Yes |       |         |
|             |          | N                                       | %     | N   | %     |         |
| Tumor type  | Breast   | 200                                     | 95.7% | 9   | 4.3%  | <0.001  |
|             | GIT      | 96                                      | 96.0% | 4   | 4.0%  |         |
|             | Lymphoma | 13                                      | 56.5% | 10  | 43.5% |         |
|             | Other    | 121                                     | 89.0% | 15  | 11.0% |         |

**TABLE 6: UNIVARIATE ANALYSIS OF THE SIGNIFICANT RISK FACTORS FOR OMITTED OR UNADJUSTED POST TOXICITY MEDICATION ERROR**

| Risk factor   |                       | Omitted or unadjusted post toxicity medication error |       |     |       |        | P-value |
|---------------|-----------------------|--|-------|-----|-------|--------|---------|
|               |                       | Non  |       | Yes |       |        |         |
|               |                       | N  | %     | N   | %     |        |         |
| Protocol type | Docetaxel protocols   | 43   | 84.3% | 8   | 15.7% | <0.001 |         |
|               | FEC-100               | 54   | 72.0% | 21  | 28.0% |        |         |
|               | Gemcitabine protocols | 62   | 78.5% | 17  | 21.5% |        |         |
|               | Other                 | 149  | 87.6% | 21  | 12.4% |        |         |
|               | Paclitaxel protocols  | 44   | 81.5% | 10  | 18.5% |        |         |
| Toxicity      | Zoledronic acid       | 61   | 88.4% | 8   | 11.6% | <0.001 |         |
|               | Hematological         | 80   | 64.5% | 44  | 35.5% |        |         |
|               | non-hematological     | 4  | 57.1% | 3   | 42.9% |        |         |
|               | both types            | 10   | 58.8% | 7   | 41.2% |        |         |
|               | non or missed         | 312  | 91.8% | 28  | 8.2%  |        |         |

**TABLE 7: UNIVARIATE ANALYSIS OF THE SIGNIFICANT RISK FACTORS FOR WRONG DOSE TIME ERROR.**

| Risk factor           | Wrong dose time error |                |        |         |         |       |      |                |        |         |         |       | P-value |
|-----------------------|-----------------------|----------------|--------|---------|---------|-------|------|----------------|--------|---------|---------|-------|---------|
|                       | Non                   |                |        |         |         |       | Yes  |                |        |         |         |       |         |
| N                     | Mean                  | Std. Deviation | Median | Minimum | Maximum | N     | Mean | Std. Deviation | Median | Minimum | Maximum |       |         |
| Total number of drugs | 320                   | 7.53           | 2.70   | 8.00    | 0.00    | 13.00 | 166  | 7.91           | 3.00   | 9.00    | 0.00    | 13.00 | 0.033   |

**TABLE 8: UNIVARIATE ANALYSIS OF THE SIGNIFICANT RISK FACTORS FOR DRUG- DRUG INTERACTION ERROR.**

| Risk factor           | Drug- drug interaction error |                |        |         |         |      |      |                |        |         |         |      | P-value |
|-----------------------|------------------------------|----------------|--------|---------|---------|------|------|----------------|--------|---------|---------|------|---------|
| N                     | Mean                         | Std. Deviation | Median | Minimum | Maximum | N    | Mean | Std. Deviation | Median | Minimum | Maximum |      |         |
| Total number of drugs | 463                          | 7.6            | 2.8    | 8.0     | 0.0     | 13.0 | 23   | 9.0            | 1.7    | 9.0     | 5.0     | 12.0 | 0.014   |

**TABLE 9: UNIVARIATE ANALYSIS OF THE SIGNIFICANT RISK FACTORS FOR LAB TEST OMISSION ERROR.**

| Risk factor               | Lab test omission error |                |        |         |         |    |      |                |        |         |         |      | P-value |
|---------------------------|-------------------------|----------------|--------|---------|---------|----|------|----------------|--------|---------|---------|------|---------|
| N                         | Mean                    | Std. Deviation | Median | Minimum | Maximum | N  | Mean | Std. Deviation | Median | Minimum | Maximum |      |         |
| Number of cycles required | 278                     | 4.58           | 3.69   | 3.00    | 1       | 17 | 128  | 3.88           | 3.4    | 3.0     | 1       | 17.0 | 0.016   |

**Multivariate analysis:**

Borderline significant factors on the univariate level were further analyzed on the multivariate logistic regression model, In case there was only one significant factor on the univariate level so no further multivariate analyses could be done. The multivariate analysis was done on the following 2

errors only (inappropriate medication and unadjusted/ omitted post-toxicity medication). The protocol type was identified as predictor for the inappropriate medication error, while the toxicity type was the predictor factor for the error omitted or unadjusted post toxicity medication. As shown in **Table 10** and **Table 11**.

**TABLE 10: MULTIVARIATE ANALYSIS OF THE SIGNIFICANT RISK FACTORS FOR IN APPROPRIATE MEDICATION ERROR**

| Risk factor for inappropriate medication error | 95% CI for OR |       |       | P-value |
|--|---------------|-------|-------|---------|
|  | OR            | Lower | Upper |         |
| Protocol type                                  |               |       |       | <0.001  |
| CHOP vs Docetaxel protocols                    | 10.1          | 1.2   | 81.3  | 0.030   |
| CHOP vs FEC-100                                | 23.8          | 3.1   | 186.0 | 0.002   |
| CHOP vs FOLFOX                                 | 11.6          | 1.3   | 101.1 | 0.026   |
| CHOP vs Gemcitabine protocols                  | 7.0           | 0.9   | 55.2  | 0.066   |
| CHOP vs other                                  | 9.7           | 1.2   | 76.0  | 0.030   |
| CHOP vs Paclitaxel protocols                   | 15.1          | 1.9   | 120.6 | 0.010   |

|                         |      |     |       |       |
|-------------------------|------|-----|-------|-------|
| CHOP vs Trastuzumab     | 14.3 | 1.7 | 119.4 | 0.014 |
| CHOP vs Zoledronic acid | 1.4  | 0.1 | 12.8  | 0.791 |

**TABLE 11: MULTIVARIATE ANALYSIS OF THE SIGNIFICANT RISK FACTORS FOR OMITTED/UNADJUSTED POST TOXICITY MEDICATION ERROR.**

| Risk factor for omitted/unadjusted post toxicity medication error | 95% CI for OR |       |       |         |
|---|---------------|-------|-------|---------|
|   | OR            | Lower | Upper | P-value |
| Toxicity  |               |       |       | <0.001  |
| Toxicity (hematologic vs non-hematologic)                         | 1.36          | 0.29  | 6.37  | 0.693   |
| Toxicity (hematologic vs both types of toxicity)                  | 1.27          | 0.45  | 3.58  | 0.647   |
| Toxicity (hematologic vs non or missed toxicity)                  | 0.16          | 0.09  | 0.27  | <0.001  |

**Table 12** summarizes the relation between the risk factors and prescribing errors; in which\_: Means statistical analysis was not done on this relation X: Means statistical analysis was done and showed no significance on univariate, and multivariate logistic regression model +: Means statistical analysis was done and showed significance on univariate

regression only and not multivariate logistic regression model. ++: Means statistical analysis was done and showed significance on both univariate, and multivariate logistic regression model. Not done: Means the number of positive cases containing the error was too small for the univariate analysis to be done.

**TABLE 12: THE RELATION BETWEEN THE RISK FACTORS AND PRESCRIBING ERRORS**

| Risk factor   | Tumor type | Tumor stage | Intention of TTT | Protocol type | Number of cycles | Course number in cycle | Dose frequency | Total number of drugs | Toxicity |
|---|------------|-------------|------------------|---------------|------------------|------------------------|----------------|-----------------------|----------|
| Inappropriate medication                                    | +          | X           | X                | ++            | -                | -                      | -              | -                     | X        |
| Unidentified protocol                                       | -          | -           | -                | -             | -                | -                      | -              | -                     | -        |
| Medication omission   | -          | -           | -                | X             | X                | X                      | -              | -                     | X        |
| Omitted/ unadjusted post toxicity medication                | X          | -           | -                | +             | -                | -                      | -              | -                     | ++       |
| Wrong BSA   | X          | -           | -                | X             | -                | X                      | -              | -                     | -        |
| Dose error  | X          | -           | -                | X             | -                | X                      | -              | X                     | X        |
| Dose omission   | -          | -           | -                | -             | X                | X                      | X              | -                     | X        |
| Wrong dose time   | -          | -           | -                | -             | X                | X                      | X              | +                     | X        |
| Lab test omission   | X          | -           | X                | X             | +                | X                      | X              | -                     | -        |
| Potential drug-drug interaction                             | -          | -           | -                | -             | -                | -                      | -              | +                     | -        |
| Duplicate prescription                                      | -          | -           | -                | -             | -                | -                      | -              | -                     | -        |
| Omitted or improper route of administration                 | -          | -           | -                | X             | X                | X                      | -              | -                     | -        |
| Wrong infusion volume                                       | +          | -           | -                | Not done      | -                | -                      | -              | -                     | -        |
| Improper infusion rate                                      | +          | -           | -                | Not done      | -                | -                      | -              | -                     | -        |
| Wrong follow up   | -          | -           | -                | Not done      | Not done         | Not done               | Not done       | -                     | Not done |
| Illegible hand-writing                                      | Not done   | -           | -                | -             | -                | -                      | -              | -                     | -        |
| Protocol not signed   | Not done   | -           | -                | -             | -                | -                      | -              | -                     | -        |
| Unspecified stage   | X          | -           | -                | +             | X                | X                      | -              | -                     | -        |
| Missed patient number                                       | X          | -           | -                | -             | X                | X                      | -              | -                     | -        |
| Intention of TTT was not comply with the protocol of choice | -          | Not done    | Not done         | Not done      | Not done         | -                      | -              | -                     | -        |

**DISCUSSION:** The rate of antineoplastic medication errors reported in the literature range from 0.4% to 31.9%<sup>26-29</sup>. In our study, antineoplastic medication errors occurred at a huge rate of 100% of the cases ranging from minor to major severity faults. In this study there were two types of errors under study; errors of omission, and errors of commission.

The dose omission incidence was (6.4%), this percentage was higher than that of the outpatient chemotherapy infusion units at the Dana-Farber Cancer Institute, Boston which represented (0.58%) of the cases studied, and (23%) of the total number of adverse drug events reported<sup>30</sup>. While the dose errors which was (66.2%), including the BSA erroneously calculated, or those involving inaccurate dose adjustment. This percentage was very high compared to that reported by Weingart et al in 2010, in which wrong dose involving oral chemotherapy was the most frequent type of error reported by (38.8%)<sup>31</sup>.

The omitted stage of tumor in the protocol templates represented the highest percentage error (68.2%) in this study, although the strategy of patient treatment largely depend on the tumor staging, for the protocol of choice to be best tailored to the patient. It was a big problem especially in those protocols required staging to decide their appropriateness for the case, such as Paclitaxel/ carboplatin for treatment of gynecological cancer. The results were comparable to the Regional Cancer Centre of a tertiary care hospital in South India which reported omitted diagnosis in (61%) of the total number of prescriptions studied<sup>19</sup>.

The inappropriateness of the protocol type represented (30%), which isn't a low percentage; it was largely dependent on the unspecified stage of tumor, and the lack of interest of studying the inclusion and exclusion criteria of each protocol, and the differentiation between the patients requiring dose modification, and those requiring shifting protocols.

There was no clear long and short term treatment strategy for each case. Such as the physicians

prescribing FEC-100 protocol for patients requiring FEC-100/Docetaxel/ Trastuzumab protocol. The chemotherapy medications Methotrexate, Etoposide, Doxorubicin, Cyclophosphamide, and Vincristine were among the top 10 drugs in the United States Pharmacopeia MEDMARX database; a national, voluntary, Internet accessible error reporting system, for all error reports from 1999 through 2004 that involved chemotherapy TTT<sup>32</sup>.

The medication omission data occurred at the percentage of (26.6%), this percentage was comparable as In Diaz-Carrasco et al retrospective study in which incorrect dose was (38.5%), and drug omission was (21.5%)<sup>33</sup>.

The drug- drug interaction occurred at a level of (4.6%), this percentage was very low compared to that reported by Riechelmann et al., in 2007, in which the percentage of drug-drug interaction was (27%)<sup>23</sup>. The low percentage of this error in our study might be a reflection of the omitted medications.

Outcomes in these studies largely depended on the study design and the definition of medication error. Nine risk factors were identified as predictors of oncology medication errors based on a number of 500 patients, but only five of them were proved to be predictors through our study.

In our study, it was an aim to find predictors for the prescribing errors in the oncology department; therefore each risk factor was studied on a number of errors, which was thought there would be a relation between them.

The risk factor (protocol type), was a predictor of the errors inappropriateness of medication, unspecified stage, and omitted/unadjusted post toxicity medication. FEC-100 protocol prescriptions were the highest increasing inappropriateness, and decreasing unspecified staging. A possible explanation because it was mainly prescribed for breast cancer patients, which the physicians of the CCC were more expertized about this type of cancer diagnosis and staging, while this protocol was prescribed regardless its' exclusion criteria such as the patient age  $\leq$  60 years, and having lymph node metastases. Ranchon

et al., in 2012 proved that the Carboplatin prescriptions were associated with increasing the dose calculation errors<sup>17</sup>.

Whereas the risk factor (the number of cycles required for each protocol) was a predictor of the error lab test omission, as the physicians were not keen of doing the lab test before each cycles, especially in those patients requiring protocols for more than three cycles.

The risk factor (toxicity type) was a predictor of the error unadjusted or omitted post toxicity medication, in which the odds of omitting added post toxicity medications is 6.25 times more if toxicity is hematological than if no toxicity was experienced by the patient. The physicians ignored the hematological toxicity experienced by the patients, especially those suffering anemia, as its treatment could increase nausea, and vomiting of the patients, while in case of neutropenia toxicity, physicians were confused about either to add filgrastim, or to delay the dose, or to reduce the dose, as well as the percentage of dose reduction.

The risk factor (total number of drugs in the protocol including pre-medications, post-medications and antineoplastic medication) was a predictor of wrong time of dose, and potential drug-drug interaction, that was because by increasing the number of drugs received by the patient that gave more chance for drug interaction between them, therefore toxicity of the protocol increased, and both the physician, and the patient became confused about receiving the next time of antineoplastic cycle. Although the finding that increasing number of medications was a risk factor for potential drug-drug interactions is consistent with previous studies<sup>19</sup>. It's surprisingly that it increased the wrong dose time in this study.

The risk factor (tumor type) was a predictor of inappropriate medication, in which, GIT department was the highest suffering that error, as FOLFOX-4 protocol [Oxaliplatin 85mg/m<sup>2</sup> day(d)(1,15), Leucovorin 200 mg/m<sup>2</sup>/day (d1,2,15,16), 5-Fluorouracil 400 mg/m<sup>2</sup>/day (d1,2,15,16) and 5-Fluorouracil 600 mg/m<sup>2</sup>/22 hour] wasn't found on the BCCA data base. On the other hand lymphoma tumor was highest tumor type

leading to wrong infusion volume, and wrong infusion rate of about (52.2%), and (43.5%) respectively, that was because CHOP protocol templates of Ain Shams University central clinic (which was prescribed to about 50% of the lymphoma cases) showed a discrepancy with BCCA protocol template.

The present study suffered several limitations including:

- The study was done on a single university hospital.
- The missed data, it was the biggest challenge in our study.
- The protocol templates were compared to BCCA data base only.

**CONCLUSION:** Our study declares that prediction of prescribing errors is feasible throughout observing the effect of risk factors on the error incidence to improve the quality and efficacy of treatment. It is clearly obvious that the treatment of oncology patient should be computerized to avoid as possible errors for example BSA calculation and therefore dose errors<sup>34</sup>. Also the role of clinical pharmacist should be expanded, and the physician, pharmacist, nurse should work in health care team, in order to decrease the errors involving medications choice, doses, drug interactions, and administration of medications<sup>35</sup>.

**ACKNOWLEDGEMENT:** We as authors would like to thank the medical, pharmaceutical, and nursing teams of the oncology department, Ain Shams university teaching hospital, for their help, and support.

**CONFLICTS OF INTERESTS:** None declared. No direct funding was received for this study.

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**How to cite this article:**

Barakat HE, Sabri NA and Saad AS: Prediction of Chemotherapy Prescribing Errors for Oncology Patients. *Int J Pharm Sci Res* 2016; 7(8): 3274-83. doi: 10.13040/IJPSR.0975-8232.7(8).3274-83.

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