Nurses' Awareness and Perception of Drug-Drug and Drug-Food Interactions

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ABSTRACT

Context: The issue of drug interactions is a global concern. Studies reported a high prevalence of drug interactions worldwide. The drug-drug interaction (DDIs) and drug-food interactions (DFIs) are often predictable and preventable. Nurses play essential roles in inpatient drug safety.

***Aim*:** This study aimed to assess nurses' awareness and perception of drug-drug and drug-food interactions.

Methods: A cross-sectional descriptive design was used to achieve the aim of this study on a convenient sample of 150 nurses working at emergency departments(medical, surgical), cardiac care unit, renal department, general surgery department, and the chest and heart surgical department at the Main University Hospital of Alexandria, Egypt. Four study tools used. They were a structured interview questionnaire designed to assess the nurses' sociodemographic characteristic, nurses' working experiences to drug-drug and drug-food interactions, and nurses' history in encountering drug-drug and drug-food interactions; nurses' awareness of drug/drug interaction assessment questionnaire, nurses' awareness of drug/food interaction assessment questionnaire, and drug safety nurses' perception assessment questionnaire.

Results: The findings of the current study reveal that 64% of the studied nurses did not receive training on DDIs or DFIs other than that in their basic education. 56% of the nurses came across patients who experienced either DDIs or DFIs. Regarding awareness, around half of them did not make aware of the drug-drug interactions of the studied drug pairs that are frequently used in the clinical practice. Concerning DFIs, 74% of the studied nurses had a low level of total awareness. Regarding nurses' perception to drug safety, 49.3% of the studied nurses agreed that the risk of drug-drug interaction is high, 55.3% agreed with the importance for prescribers to learn about DDIs and DFIs, and 53.3% of them agreed with the information regarding the DDIs and DFIs useful to the nurse in plan management. The current study revealed a statistically significant association between training received and nurses' awareness regarding DDIs and DFIs.

Conclusion: The study concluded a low level of awareness among the studied nurses regarding DDIs and DFIs with an average perception of the risk of DDIs/DFIs, and the importance of related information in plan management. The study recommended different strategies to be applied to assist prescribers and nurses in identifying potential DDIs, providing educational interventions, facilitating access to DDI information sources, applying computerized alerting systems, and delivering performance feedback among the most commonly recommended strategies.

Keywords: Nurses' awareness, perception, drug-drug, drug-food interaction.

1. Introduction

The term "drug interaction" is most often used to describe drug-drug interactions (DDI), but there are various substances such as food, drink, herbal medicine, nutritional supplements, and other environmental chemicals that can alter the pharmacokinetics or pharmacodynamics of medications*(Thanacoody, 2012; Frandsen &Pennington, 2014; Karahan et al., 2015).*Depending on the effect of the DDI on patients, the DDI can be classified into beneficial, harmful or neutral, or may be fatal in some cases. The mechanism of DDI includes inhibition or induction of drug-metabolizing enzyme, inhibition of drug transporters, and competition on plasma albumin, which can affect the pharmacokinetic parameters*(Palleria et al., 2013).*

A comprehensive definition of drug-food interaction (DFIs) is an interaction resulting from a physical, chemical, physiologic, or pathophysiologic relationship between a drug and a nutrient, multiple nutrients, food in general, or nutritional status *(Ötles & Senturk 2014).* Interactions between food and drugs may accidentally reduce or increase the drug effect. The majority of clinically relevant food-drug interactions are caused by food-induced changes in the bioavailability of the drug. Major side-effects of some diet (food) on drugs include alteration in absorption by fatty, high protein, and fiber diets. Bioavailability is an important pharmacokinetic parameter that is correlated with the clinical effect of most drugs *(Bushra et al., 2011; Piscitelli et al., 2011).*

The issue of drug interactions is a global concern. *Ahmad et al. (2015)* reported that 30.3% of patients were at risk of DDIs in the ambulatory care unit. Other studies have also reported a high rate of prevalence of 1-3% drug interactions worldwide. Drug-drug interactions (DDIs) present an ever-evolving challenge and still critical safety issues in disease management. According to the Food and Drug Administration, 3%-30% of patients experienced drug-drug interaction (*Food and Drug Administration,*

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2009; Karahan et al., 2015). It is reported that DDI accounted for causing 4.8% of total hospitalization cases, which increases the medical costs and mortality among patients *(Palleria et al., 2013).*

Khan et al. (2014) reported the exposure to potential drug-drug interaction in teaching hospitals in Pakistan that among 100 prescriptions (543 medicines), 41% of prescriptions have potential DDI's. The survey showed the severity level accounting as major (20.1%), moderate (63.4%), and minor (15.90). *Kothari and Ganguly (2014)* portrayed a meta-analysis of 23 clinical studies from around the world reported that DDIs cause emergency room visits, hospital admissions, and re-hospitalizations. DDIs were associated with a lack of medication efficacy, poor tolerability, serious adverse events, negative clinical outcomes, and increased healthcare costs. Besides, additive respiratory depression, bleeding risk, reduced iron absorption, and central nervous system depression *(Roblek, 2015).*

A recent meta-analysis of 13 studies found that DDIs are responsible for approximately 1.1% of hospital admissions, and 22.2% of all Adverse Drug Reactions (ADRs) leading to admission are caused by DDIs *(Dechanont et al., 2014).* Due to population aging and increasing polypharmacy, these ratios are expected to increase. According to a Scottish study, the proportion of adults dispensed ≥5 drugs doubled to 20.8% between 1995 and 2010, and the proportion of those dispensed ≥10 tripled to 5.8%. The prevalence of potentially serious DDIs went up to 13%, a more than twofold increase during the same period *(Guthrie et al., 2015).*

Schrecker et al. (2018) conducted a study on 1500 patients aimed to detect objectively the recently ingested substances in urine with subsequent identification of DDIs. Of note, around 11% of these interactions were identified as severe or contraindicated. Another important study conducted on 262 patients with pain, behavioral disorders, or both. The patients were objectively tested for DDIs, and their medical record was compared prior and after a drug interaction was identified. The results of the study revealed a significant reduction in outpatient visits per month and reducing costs by 22% *(Arnold et al., 2018).* The DDIs are often predictable and preventable. The prevalence and incidence of clinically observable DDIs are between 5-10%, and up to 25% of patients on pharmacological treatment, and potential DDIs is at least three to five times higher (from 15% to 50%) *(Turabian, 2019).*

Nurses spend about 40% of their time on the preparation of medications. Therefore, they play a chief role in patients' medication process. According to recent research, medication errors originate from physicians in 39% of the cases, from nurses in 38% and pharmacists in 23% of cases *(Atari et al., 2017).* DDIs are a real problem in clinical practice, which may partly remain hidden *(Turabian, 2019).*

Several studies confirm that registered nurses play essential roles in patient safety *(Institute of Medicine (IOM) Recommendations, 2010; Agency for Health Care Research and Quality (AHRQ) 2007).* The Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) requires a thorough drug history be taken during hospital admission, as well as adequate drug reconciliation during discharge *(Unroe et al., 2010).* JCAHO recommends that nurses should be alert in monitoring for possible DDIs and DFIs, provide guidance to patients on food and beverages to avoid when on certain medications. Nurses have to be adequately trained and be current on possible DDIs and DFIs to function effectively in this role *(Enwerem et al., 2017).*

Nurses play a significant role in medication safety as patients' advocates. Hence, they must be aware of the pharmacological principles for each drug; the regulations of drug management; precautions for preparation; and considerations of administration to patients and must be able to identify the possible DIs so that patients are not exposed to unwanted situations *(Enwerem, & Okunji, 2017; Simonsen et al., 2014; Faria, & Cassiani, 2011)*. Nurses are uniquely positioned in the prevention of drug interactions *(Karahan et al., 2015).*

2. Significance of the study

Every year thousands of drugs are being introduced in the market, which results in numerous new interactions between medications reported annually (*Amirthalingam & Vaidhun, 2010).* Despite the overwhelming effect of drug interactions and increased prevalence of these deleterious health outcomes attributed to drug interactions *(Gebretsadik et al., 2017),* given the ever-changing and expanding information about medications, poly pharmacy rise in multi morbidity, use of evidence-based clinical guidelines and care pathways, and a focus on disease prevention *(Kaufman, 2016).* It has been observed only a small number of literature foresight the evidence about health care professionals on DDIs and DFIs knowledge *(Ali et al., 2017).*

Although several studies have evaluated the frequency and ramifications of medication errors, few have investigated their causes. Mainly, nurses' knowledge regarding drug-drug and food-drug interactions has been evaluated minimally. Little is known about nurses' knowledge regarding this phenomenon. An Egyptian study reported that the prevalence of DDIs among patients admitted to CCUs was 53.07%. The mean number of interactions that occurred per patient was 2.98±1.91 interactions. The most common interaction reported was 47.99% for Clopidogrel and Aspirin, 45.23% for Clopidogrel and Atorvastatin and 40.45% for Furosemide and Aspirin. Age of the patient and the number of prescribed drugs were the two independent factors found to be significantly affecting the prevalence of DDIs *(Mohamed et al., 2015).* Therefore, this study aims to assess the nurses' awareness and perception of drug-drug and drug-food interactions.

3. Aim of the study

This study aimed to assess nurses' awareness and perception of drug-drug and drug-food interactions.

- What is the level of nurses' awareness of drug-drug interaction?
- What is the level of nurses' awareness of drug-food interaction?
- What is the level of nurses' perception of drug safety (drug-drug and drug-food interaction)?

4.Subjects & Methods

4.1. Research design

The present study follows a cross-sectional descriptive design to achieve the aim of this study. Cross-sectional studies are observational and are known as descriptive research. Researchers record the information that is present in a population, but they do not manipulate variables. This method is often used to make inferences about possible relationships or to gather preliminary data to support further research and experimentation *(Cherry & Gans 2019).*

4.2. Research Setting

The study conducted at the Main University Hospital (medical, surgical departments). Medical departments include cardiology, nephrology, endocrinology, gastroenterology, geriatrics and medical oncology. Surgical departments as urology, neurosurgery, cardiac surgery, vascular surgery, plastic surgery and gastrointestinal surgery. Total number of working nurses in the above-mentioned settings was 300 nurses who provided direct contact to the patients.

4.3. Subjects

A convenient sample of 150 nurses who worked at the above-mentioned clinical settings regardless of their age, qualifications, or years of experience. They were distributed on the three working shifts.

Epi info program v 7.0 was used to find the sample size by applying the following parameters: Expected frequency 50%, acceptable error 5%, confidence coefficient 95%, population size 300 nurses, and minimum sample size 150 students.

4.4. Tools of the study

4.4.1. A Structured Interview Questionnaire for Studied Nurses

It developed by the researchers based on *Ahmad et al. (2015); Ali et al. (2017)*; *Attari et al. (2017)*; *El Lassy and Ouda, (2019); Moges, (2013)* to assess the nurses' sociodemographic characteristics, nurses' working experience with drug-drug interaction, and nurses' history of encountering drug-drug interactions. The sociodemographic characteristics of nurses under study included nurses' gender, age, educational level, practice setting, and area of specialization.

The second part was concerned with the nurses' work experience in drug-drug/drug-food interactions. It included 6(closed and open-end) questions related to receiving training on drug-drug/drug-food interactions other than that of formal education, the average number of patients seen by the nurse per day, working hours per week, the average number of administrating prescriptions per day.

The third part was concerned with nurses' history in encountering drug-drug/drug-food interactions during clinical practice. It included two (close and open-end) questions related to encountering a patient who had drug-drug/drug-food interactions that caused adverse outcomes, with a subsequent question regarding the numbers of events, and the consequent adverse outcomes, and the familiarity with the standards treatment guidelines in the hospitals.

4.4.2. Nurses' Awareness of Drug/Drug Interaction Assessment Questionnaire

It was adopted from *Moges, (2013)* to assess the nurses' awareness of drug/drug interactions. It included 15 questions related to the 15 pairs of drugs that interacted when given together. The studied pairs were Acetaminophen with Codeine and Amoxicillin, Carbamazepine and Clarithromycin, Digoxin and Verapamil, Digoxin and Clarithromycin, Digoxin and Sildenafil, Metformin and Erythromycin, Nitroglycerin and Sildenafil, Simvastatin and Itraconazole, Warfarin and Cimetidine, Atenolol and Ranitidine, Carbamazepine and Cimetidine, Warfarin and Fluconazole, Allopurinol and Pyrazinamide, Praziquantel and Rifampicin, and Warfarin with Cotrimoxazole. Each question is answered against the three-points scale of sure (contraindicated), not sure (could be used under monitoring), and does not know (do not know about the possibility of interaction).

Scoring system

Each pair of drugs is subjected to one of the three previous responses as sure, given three scores, two scores for not sure, and one score for do not know. The total score was 45 points. It was converted into percent score that classified as less than 60% considered as low awareness, ≥60%-75% considered as moderate awareness, and > 75% considered as high awareness.

4.4.3. Nurses' Awareness of Drug/Food Interaction Assessment Questionnaire

It was developed by the researchers based on *Thanacoody, (2012); Frandsen & Pennington, (2014)* to assess the nurses' awareness of drug/food interactions. It included 13 questions related to drug-food interactions. The drug-food studied pairs were Digitalis and high fiber food, Levodopa and high protein food, Methyldopa and high protein food, Penicillamine and dairy products or iron-rich food or supplements, Tetracycline and milk, Cephalosporins and fruit juices or wine; antihypertensive, heart medications, antiarrhythmics, and caffeine; Asthma drugs (Pseudoephedrine, Theophylline), caffeine and high fiber diet, Cholesterol-lowering drugs (Cholestyramine, Gemfibrozil) and fatty foods; Peptic ulcer medications (Antacids, Cimetidine, Famotidine, Sucralfate) with caffeine and high fiber diet; hormones (Thyroid drugs) and Iodine-rich food, painkillers (Aspirin, NSAID) and alcohol, Codeine and low fiber diet and low water. Each

combination is subjected to one of the three responses. They were sure (contraindicated), not sure (could be used under monitoring), and do not know (do not know about the possibility of interaction).

Scoring system

Each drug and food combination were subjected to one of the three previous responses as sure, given three scores, two scores for not sure, and one score for do not know. The total score was 39 points. It was converted into percent score that classified as less than 60% considered as low awareness, ≥60%-75% considered as moderate awareness, and >75% considered as high awareness.

4.4.4. Drug Safety Nurses' Perception Assessment Questionnaire

It was developed by the researchers based on *Thanacoody, (2012); Frandsen and Pennington, (2014); Bertoli et al. (2010)* to assess the nurses' perception of drug safety, including the safety of drug-drug and drug-food interactions. It included seven statements assessed the nurses' perception toward drug safety through assessment of their perception of drug-drug and drug-food interactions such as the risk of drug-drug and drug-food interaction is high, learning about drug-drug and drug-food interaction is important. It is the responsibility of the pharmacist to consider drug-drug/drug-food interactions. The statements were subjected to a four-point scale ranged from disagreeing, somewhat disagree, somewhat agree, to agree.

Scoring system

Each statement is subjected to one of the four previous responses as four scores for agreeing, three scores for somewhat agree, two scores for somewhat disagree, and one score for disagree. The total score was 28 points. It was converted into percent score that classified as less than 60% considered as low awareness, ≥60%-75% considered as moderate awareness, and >75% considered as high awareness.

4.5. Procedures

The researcher developed the study tools after extensive reviewing of relevant literature, the content of the tools revised by a panel of three experts in the medical surgical nursing department at faculty of nursing, Alexandria University and two professors of pharmacology at Faculty of Medicine Alexandria University to test the content validity, completeness and clarity of tools. Comments and suggestions were considered, and the tools were modified accordingly. The reliability of the developed tools was tested by (analogous to Cronbach's Alpha coefficient) was 0.65, 0.70, and 0.75 for nurses' awareness of drug/drug interactions assessment questionnaire, nurses' awareness of drug/food interactions assessment questionnaire, and drug safety nurses' perception assessment questionnaire.

Ethical consideration: The approval for data collection was obtained from the institutional review board of Main Alexandria University Hospital, Alexandria University. A cover letter was attached to each of the questionnaires. The questionnaires were attached with a participant information data to be filled in and an explanation regarding the research process. Oral approval was obtained from nurses who were participating in the study.

The participation of all subjects implied consent by completing and returning the questionnaires to the researcher. Information was stored on the researchers' personal computers. Participant's confidentiality was assured as nurses' names were written elective. Each participant has the right to terminate the process anytime. The researcher assured the participants that the issues raised, and their responses would be kept confidential and would not be included in any job evaluation.

A pilot study was conducted on 15 nurses (10% of the target sample) to ensure the clarity and applicability of the tool and identify the feasibility of the research process. The pilot sample was not included in the study. The fieldwork started by visiting the study units consecutively. The researchers visited each study unit two/days a week (Sunday and Monday). The range of nurses met each day ranged between 3-4 nurses.

Nurses were interviewed separately during the end of the clinical shift. The interview ranged from 15 to 20 minutes for each nurse. The interview started with an explanation of the study's aim and benefit from the research. Then the researcher administered the structured interview questionnaire to collect the nurses sociodemographic; then, they complete the awareness assessment questionnaires. Data collection was performed for over five months (from March 2019 to July 2019).

4.6. Data analysis

Data were fed to a personal computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using the number and percent. Quantitative data were described using the range (minimum and maximum), mean, and standard deviation. The significance of the obtained results was judged at the 5% level. The statistical analysis was done using a student t-test applied when the test statistic follows a normal distribution. F-test (ANOVA) used for the normally distributed quantitative variables to determine whether the variability between group means is larger than the variability of the observations within the groups. Pearson coefficient to correlate between two normally distributed quantitative variables is a measure of the linear correlation between two variables *X* and *Y*.

5. Results

Table 1 shows that 81.3% of the studied nurses were females, with a mean age of 33.70 ±10.43. 47.3% of them had a technical diploma, 90% of them were working in a governmental hospital, and 52% of the working in the emergency medicine department.

Table 2 shows that 64% of the studied nurses did not receive training other than that in their basic education, among 36% of the trained studied nurses, 24% of them trained through the workshops and seminar, and 12%

through lecturing regarding treatment interaction. 56.7% of the nurses cared for 15-20 patients daily, while 32.7% cared for less than 15 patients per day. 60% of nurses spend 31-40 hours in hospital per week, and 30% of them spend more than 41-50 hours per week. 52% of the studied nurses administer between 10-20 prescriptions per day, while 47.3% gave less than ten prescriptions per day.

Table 3 demonstrates the nurses' history of encountering drug-drug and drug-food interaction. 56% of the nurses came across patients who experienced either a drug-drug or drug-food interaction; among them, 34% encountered it twice, 29.8% encountered it once, 25% encountered it several times. Also, 45.2% of the nurses who encountered a drug-drug or drug-food interactions were observed nausea and vomiting, 41.7% observe dysrhythmias, and 36.9% observe dizziness, 22.6% observed hypotension, 16.7% observed changes in blood pressure among the adverse outcomes of drug-drug or drug-food interactions. 50% of the studied nurses reported familiarity with the standards of hospital treatment guidelines; among them, 53.3% were somewhat familiar.

Table 4 reveals that 58.6% of the studied nurses did not know about the drug-drug interaction (DDI)of Warfarin and Fluconazole, 56% did not know about the DDI of Digoxin and Clarithromycin, 55.7% did not know about DDI of Carbamazepine and Clarithromycin, 55.4% did not know about the DDI of Metformin and Erythromycin and DDI of Allopurinol and Pyrazinamide. Also, 55.3% of the nurses did not know about the DDI of Warfarin and Co-trimoxazole; 54.7 % of them did not know about the DDI of Digoxin and Sildenafil. Besides, 52.6 of them did not know the DDI of Carbamazepine and Cimetidine, 51.3% did not know about the DDI of Digoxin and Verapamil, 50.7% of them did not know about the DDI of Praziquantel and Rifampicin, and 50.6% of them did not know about the Atenolol and Ranitidine.

Table 5 represents the nurses' awareness of drug-food interaction. 47.3% of the studied nurses did not know the drug-food interaction (DFIs) of digitalis and high fiber diet, and the DFI of Levodopa and high protein diet. Also, 42.7% of them did not know about the DFIs of Methyldopa and high protein diet. On the other hand, 57.3% of the studied nurses were not sure about the DFIs between asthma drugs, caffeine, and high fiber diet, 50% were not sure about the DFIs between Cephalosporines and fruit juice or wine, 49.3% were not sure about the DFIs of Penicillamine and dairy products or iron-rich foods or supplements, and between Tetracyclines and milk. On the contrary, 47.3% of the studied nurses were sure about the DDIs of antihypertensive, antiarrhythmic drugs and caffeine, 41.3% of them were sure about the DFIs between the cholesterol-lowering drugs and fatty foods.

Table 6 clarifies the nurses' perception of drug safety regarding DDI and DFIs. The table shows that 55.3% of the studied nurses agreed with the importance of prescribers to learn about DDIs and DFIs. Also, 53.3% of them agreed about the accurate information regarding the DDIs and DFIs useful to the nurse in plan management, and 50.7% were agreed about the responsibility of the pharmacist to consider DDIs and DFIs. On the same line, 49.3% of the studied nurses perceive that the risk of drug-drug interaction is high, 49.3% is agreed somewhat that the information regarding DDIs and DFIs is relevant to patient safety, and 42.7% of them perceive somewhat that the nurse is likely to consider DDIs and DFIs as a part of their decision.

Table 7 reveals a low total nurses' awareness of drug-drug interaction among 49.3% of the studied nurses and 74% regarding DFIs. While 68.7% of the studied nurses were highly perceived the drug safety regarding the DDIs and DFIs.

Table 8 shows a statistically significant positive correlation between nurses' perception of drug safety and nurses' awareness of drugs-food interactions, while there is a non-statistically association between the nurses' perception of drug safety and nurses' awareness of DDIs.

Table 9 demonstrates a highly statistically significant association between nurses' educational levels, perception, and awareness to DDIs and FDIs as the highest mean scores were for the Bachelor degree nurses in both perception and awareness to FDIs while the highest mean score was for diploma nurses regarding DDIs. Also, there was a highly statistically significant association between the practice setting and the awareness of DDIs as the nurses working in a governmental hospital had a higher mean score.

A statistically significant association was found between the area of specialization and both perception and awareness of DDIs and DFIs as nurses in the renal department, and emergency surgery had the highest mean scores of perception of drug safety. In contrast, the nurses in internal medicine, chest, and heart surgery represented the highest mean score of awareness to drug-drug interaction. The nurses in internal medicine and emergency surgery had the highest mean scores of awareness of drug-food interactions.

Table 10 shows a statistically significant difference association between training received and nurses' awareness of DDIs and DFIs with those who receive training had the highest mean scores. Also, a statistically significant association was revealed between the type of training, and both perception of drug safety and the awareness of DDIs with those who received lecturing regarding the treatment interaction had the highest mean scores. Besides, there was a statistically significant difference between the average number of patients cared for by the nurse per day and the nurses' perception of drug safety with the nurses who cared for less than 15 patients per day had the highest mean score.

A statistically significant difference was revealed between hours spent by the nurses in the hospital, and their awareness of DDIs and DFIs with the nurses who spend between 20-30 hours had the highest mean. Also, A highly statistically significant difference was revealed between the average number of prescriptions the nurse administered per day and DFIs with the nurses who gave the highest number of prescriptions had the highest mean score of FDIs.

Table (1): Frequency and percentage distribution of the studied nurses according to their socio-demographic characteristics (n = 150).

Variables	No. (150)	%
Gender		
Male	28	18.7
Female	122	81.3
Age (years)		
<30	62	41.3
30-40	32	21.3
40-50	36	24.0
≥50	20	13.3
Min. – Max.	18.0 – 57.0	
Mean ± SD.	33.70 ±10.43	
Education level		
Technical diploma	71	47.3
Bachelor	44	29.3
Master	2	1.3
Other	33	22.0
Practice setting		
Governmental hospital	135	90.0
Private hospital	0	0.0
At both	15	10.0
Area of Specialization		
Emergency surgery	9	9.0
Emergency medicine	78	52.0
Cardiology	19	12.7
Internal medicine	36	24.0
Renal department	8	5.3
Chest and heart Surgery	5	3.3
General Surgery	3	2.0

Table (2): Frequency and percentage distribution of the studied nurses according to their working experience in drug-drug and drug-food interactions (n = 150).

Variables	No.	%
Nurses received training on drug-drug or drug-food interactions other than in their basic education		
Yes	54	36.0
No	96	64.0
Type of training if any		
Workshops, seminars regarding treatment interactions	36	24.0
Lectures regarding treatment interactions	18	12
The average number of patients cared for by the nurse per day		
<15	49	32.7
15-20	85	56.7
21-30	14	9.3
>30	2	1.3
Average hours the nurse spend in the hospital per week		
<20	8	5.3
20-30	4	2.7
31 -40	90	60.0
41-50	45	30.0
>50	3	2.0
The average number of prescriptions the nurse administers per day		
<10	71	47.3
10-20	78	52.0
21 -30	1	0.7
>30	0	0.0

Table (3): Frequency and percentage distribution of the studied nurses according to their history of encountering drug-drug and drug-food interactions (n = 150).

Variables	No.	%
The nurse came across a patient who had a drug-drug/drug-food interaction that caused adverse outcomes.		
Yes	84	56.0
No	66	44.0
The frequency of encountering drug-drug and drug-food interactions if any (n=84)		
Once	25	29.8
Twice	29	34.5
Three-time	9	10.7
Several times	21	25.0
The adverse outcomes encountered by the nurses as a result of drug-drug or drug-food interactions(n=84)		
Intoxication/ over dosage	11	13.1
Bleeding	7	8.3
Hypotension	19	22.6
Therapeutic failure	5	6.0
Nausea/vomiting	38	45.2
Dizziness	31	36.9
Headache	11	13.1
Dysrhythmias	35	41.7
Change in blood pressure	14	16.7
Skin rash	8	9.5
Allergy	9	10.7
Fever	4	4.8
Death	2	2.4
Dyspnea	4	4.8
Nurses' familiarity with the standards hospital treatment guidelines		
Yes	75	50.0
No	75	50.0
The extent of familiarity with the standard hospital treatment guideline		
Little familiar	28	37.3
Somewhat familiar	40	53.3
Familiar	7	9.4

Table (4): Frequency and percentage distribution of the studied nurses' awareness regards to drug-drug interactions among common pairs (n= 150).

Drug pairs	Sure		Not sure		Do Not know	
	No.	%	No.	%	No.	%
Acetaminophen with Codeine + Amoxicillin	51	34.0	26	17.3	73	48.7
Carbamazepine + Clarithromycin	39	26.0	26	17.3	85	55.7
Digoxin + Verapamil	36	24.0	37	24.7	77	51.3
Digoxin + Clarithromycin	34	22.7	32	21.3	84	56.0
Digoxin + Sildenafil	30	20.0	38	25.3	82	54.7
Metformin + Erythromycin	34	22.7	33	22.0	83	55.4
Nitroglycerin + Sildenafil	39	26.0	38	25.3	73	48.6
Simvastatin + Itraconazole	34	22.7	42	28.0	74	49.3
Warfarin + Cimetidine	35	23.3	42	28.0	73	48.7
Atenolol + Ranitidine	34	22.7	40	26.7	76	50.6
Carbamazepine + Cimetidine	38	25.3	33	22.0	79	52.6
Warfarin + Fluconazole	34	22.7	28	18.7	88	58.6
Allopurinol + Pyrazinamide	37	24.7	30	20.0	83	55.4
Praziquantel + Rifampicin	41	27.3	33	22.0	76	50.7
Warfarin + Co-trimoxazole	42	28.0	25	16.7	83	55.3

Table (5): Frequency and percentage distribution of the studied nurses' awareness regards to drug-food interactions (n= 150).

Drugs	Food interacting	Sure		Not sure		Do not know	
		No.	%	No.	%	No.	%
Digitalis	High fiber food	16	10.7	63	42.0	71	47.3
levodopa	High-protein food	20	13.3	59	39.3	71	47.3
Methyldopa	High-protein food	22	14.7	64	42.7	64	42.7
Penicillamine	Dairy products or iron-rich foods or supplements	15	10.0	74	49.3	61	40.7
Tetracyclines	Milk	27	18.0	74	49.3	49	32.7
Cephalosporins	Fruit juice or wine	26	17.3	75	50.0	49	32.7
Antihypertensives, antiarrhythmic drugs	Caffeine	71	47.3	47	31.3	32	21.3
Asthma drugs (Pseudoephedrine Theophylline)	Caffeine and a high fiber diet	35	23.3	86	57.3	29	19.3
Cholesterol-lowering drugs (Cholestyramine, Gemfibrozil)	Fatty foods	62	41.3	57	38.0	31	20.7
ulcer medications (Antacids Cimetidine Famotidine, Sucralfate)	Caffeine and a high fiber diet	39	26.0	70	46.7	41	27.3
Hormone preparations (Thyroid drugs)	Iodine-rich foods	55	36.7	53	35.3	42	28.0
Painkillers aspirin and more potent nonsteroidal anti-inflammatory drugs	Alcohol	58	38.7	53	35.3	39	26.0
Codeine	Need fiber and water intake	24	16.0	69	46.0	57	38.0

Table (6): Frequency and percentage distribution of the studied nurses' perception of drug safety regarding drug-drug and drug-food interactions (n= 150).

Variables	Disagree		Somewhat disagree		Somewhat agree		Agree	
	No.	%	No.	%	No.	%	No.	%
The risk of drug-drug and drug-food interactions is high	7	4.7	21	14.0	48	32.0	74	49.3
Prescribers need to learn about drug-drug/drug-food interactions	3	2.0	16	10.7	48	32.0	83	55.3
It is the responsibility of the pharmacist to consider drug-drug/drug-food interactions	17	11.3	12	8.0	45	30.0	76	50.7
The nurse is likely to consider drug-drug/drug-food interactions as part of the nurses' decisions	5	3.3	16	10.7	64	42.7	65	43.3
The drug-drug/drug-food interactions information relevant to patient safety	15	10.0	8	5.3	74	49.3	53	35.3
The drug-drug/drug-food interactions information sufficient for the nurse to manage the interaction	6	4.0	20	13.3	62	41.3	62	41.3
The drug-drug/drug-food interactions accurate information useful to the nurse in plan management	7	4.7	7	4.7	56	37.3	80	53.3

Table (7): Frequency and percentage distribution of the studied nurses' total awareness of drug-drug, drug-food interactions, and their perception of drug safety (n = 150).

Variables	High (>75%)		Moderate (60 – 75%)		Low (<60%)	
	No.	%	No.	%	No.	%
Nurses' drug-drug interactions awareness	60	40.0	16	10.7	74	49.3
Nurses' drugs-food interaction awareness	11	7.3	28	18.7	111	74.0
Nurses' perception of drug safety (DDIs and DFIs)	103	68.7	20	13.3	27	18.0

Table (8): Correlation between assessment of nurses' awareness &perception on drug-drug interactions, drug-food interaction (n = 150)

Variables	Mean± SD	r	p
Nurses' perception of drug safety Vs nurses' awareness of drug-drug interactions	22.82 ± 3.95 41.03 ± 15.86	-0.085	0.302
Nurses' perception of drug safety Vs nurse awareness of drug-food interactions	22.82 ± 3.95 26.85 ± 7.03	0.364	<0.001
Nurses' drug-drug interactions awareness Vs nurse awareness of drug-food interactions	41.03 ± 15.86 26.85 ± 7.03	-0.017	0.836

r: Pearson coefficient, Statistically significant at p ≤ 0.05

Table (9): Relationship between sociodemographic characteristics and total perception of drug safety and awareness of drug-drug and drug-food interactions.

Variables	Nurses' perception of drug safety (DDIs and DFIs)	Nurses' awareness of drug-drug interactions	Nurses' awareness of drug-food interactions
	Mean ± SD.	Mean ± SD.	Mean ± SD.
Sex			
Male	23.79 ± 3.35	38.54 ± 10.12	26.0 ± 5.91
Female	22.60 ± 4.05	41.61 ± 16.89	27.04 ±7.27
t(p)	1.440 (0.152)	1.254 (0.214)	0.705(0.482)
Age (years)			
<30	23.35 ± 3.68	40.79 ± 14.12	26.63 ± 6.31
30-40	22.66 ± 4.03	44.16 ± 17.24	26.25 ± 8.06
40-50	22.42 ± 4.31	39.56 ± 18.15	26.50 ± 7.84
≥50	22.15 ± 4.02	39.45 ± 14.76	29.10 ± 5.84
F(p)	0.711(0.547)	0.584(0.626)	0.807(0.492)
Educational level			
Diploma	22.27 ± 4.41	45.79 ± 16.13	25.32 ± 8.41
Bachelor	23.98 ± 3.11	40.36 ± 11.59	28.86 ± 5.08
Master	16.0 ± 0.0	28.0 ± 0.0	21.0 ± 0.0
F(p)	3.935*(0.010*)	6.432*(<0.001*)	3.101*(0.029*)
practice setting			
Governmental hospital	22.84 ± 4.04	42.87 ± 15.23	26.75 ± 7.07
At both	22.60 ± 3.09	24.47 ± 11.47	27.73 ± 6.81
t(p)	0.227(0.821)	5.684*(<0.001*)	0.514(0.608)
Area of Specialization			
Emergency surgery	24.33 ± 1.86	37.17 ± 14.51	34.67 ± 6.28
Emergency medicine	22.37 ± 3.81	39.78 ± 17.53	26.17 ± 6.19
Cardiology	22.0 ± 4.32	42.21 ± 17.06	22.37 ± 6.34
Internal medicine	22.33 ± 9.81	60.0 ± 0.0	38.33 ± 6.35
Renal department	24.69 ± 2.55	38.81 ± 10.43	27.72 ± 5.64
Chest &heart Surgery	19.75 ± 5.12	56.25 ± 7.27	30.0 ± 12.01
F(p)	3.394*(0.006*)	2.825*(0.018*)	6.098*(<0.001*)

*t: Student t-test, F: F for ANOVA test, p-value for the association between different categories, *Statistically significant at p ≤ 0.05*

6. Discussion

Drug administration is a primary nursing task that involves competent technique and consideration of the patient's development and health status. Nurses' sufficient medication competence is highly essential for patient safety. Nurses have a significant role and accountability in providing patient's medication care successfully and securely*(Bertoli et al., 2010).*Continuing assessment is a central part of nursing care for both assessments of patient response to administered medications and early recognition of harmful effects*(Sulosaari et al., 2010).*The nurse has a unique position in the prevention of drug interactions, so this study aimed to assess nurses' awareness and perception of drug-drug and drug-food interactions.

The findings of the current study reveal that most of the nurses were females with their mean age of 33.70±10.43, around fifty percent of them had a technical diploma in nursing, the majority of studied nurses were working in a governmental hospital and more than half of them were working in emergency medicine department. In Egypt, the vast majority of nurses are predominantly females and graduated from technical nursing education; by low, they are assigned to work in governmental hospitals. Similar findings reported by *Elhada (2018),* who studied the "increasing nurses' awareness of drug interaction," and reported that most nurses were females. Most of them were staff nurses, and about two-thirds had a Bachelor degree in nursing, and one-third had a diploma in nursing.

Also, *Alkhaldi et al. (2019)* stated that the majority of nurses have a diploma in general nursing. These findings are nearly similar to *Endal et al. (2019),* in a study about health care professional awareness toward drug-drug interactions (that included 216 nurses). The study reported that around two-thirds of the participants were females, and 70% of the participants were in the age group of 26-35.An Egyptian study for "the effect drug-food interactions educational program on knowledge and practices of nurses working at the pediatric outpatients' clinics in El-Beheira General Hospital" revealed that three-fourths of the studied nurses were below the age of 35 with a mean age of 28.3±8.65, and had technical nursing diploma *(EL Lassy & Ouda, 2019).*

Training is an integral part of nursing. The findings of the current study revealed that around two-thirds of the studied nurses did not receive training on DDIs or DFIs other than that in their formal education, among those who trained, one quarter attend workshops, seminars regarding treatment interactions, and less than one-tenth had lecture regarding DDIs and DFIs. These findings are reflecting a low priority of DDIs and FDIs in hospital Inservice education program.

Table (10): Relationship between nurses' working experience and total perception of drug safety and awareness of drug-drug and drug-food interactions.

Variables	Nurses' Perception of drug safety (DDIs and DFIs) Mean ± SD.	Nurses' awareness of drug-drug interactions Mean ± SD.	Nurses' awareness of drugs-food interactions Mean ± SD.
Nurses received training on drug-drug or drug-food interaction other than in their basic education			
Yes	23.07 ± 4.17	44.70 ± 16.33	28.65 ± 8.67
No	22.68 ± 3.83	38.97 ± 15.29	25.83 ± 5.72
t(p)	0.590(0.556)	2.151*(0.033*)	2.138*(0.036*)
Type of training if any			
Workshops, seminars regarding treatment interactions	23.06 ± 3.90	40.86 ± 17.98	28.11 ± 8.04
Lectures regarding treatment interactions	24.06 ± 4.14	51.44 ± 8.53	29.19 ± 10.09
F(p)	4.191*(0.021*)	3.546*(0.036*)	0.471(0.627)
The average number of patients cared for by the nurse per day			
<15	24.12 ± 2.82	41.22 ± 10.66	26.08 ± 6.70
15-20	21.95 ± 4.31	39.94 ± 18.64	26.87 ± 7.06
21-30	23.50 ± 4.20	45.14 ± 12.96	29.93 ± 7.99
>30	23.0 ± 0.0	54.0 ± 0.0	23.0 ± 0.0
F(p)	3.446*(0.018*)	0.894(0.446)	1.298(0.278)
Average hours the nurse spend in the hospital per week			
<20	19.75 ± 6.67	45.63 ± 17.82	21.75 ± 10.10
20-30	24.25 ± 3.30	57.75 ± 4.50	42.0 ± 0.0
31 -40	23.02 ± 3.46	37.70 ± 16.72	26.54 ± 6.61
41-50	22.96 ± 4.29	44.87 ± 12.13	26.98 ± 5.95
>50	21.0 ± 1.73	49.0 ± 19.05	27.33 ± 5.77
F(p)	1.598 (0.178)	3.312*(0.012*)	6.611*(<0.001*)
The average number of prescriptions the nurse administers per day			
<10	22.14 ± 4.56	40.08 ± 17.20	27.97 ± 7.95
10-20	23.37 ± 3.19	41.65 ± 14.56	25.63 ± 5.70
21 -30	28.0	60.0	42.0
F(p)	2.736(0.068)	0.900 (0.409)	4.617*(0.011*)

*t: Student t-test, F: F for ANOVA test, p-value for the association between different categories, *Statistically significant at p ≤ 0.05*

Additionally, the training on drug issue might involve the education regarding the ten rights of drug administration, drug administration techniques but might not involve particular information regarding the DDIs and DFIs. Also, many nurses and nurses' trainers might consider that DDIs and DFIs are not nurses' concerns or even a significant issue. All these factors might hinder the nurses' awareness of this vital point of drug management.

Endal et al. (2019) reported similar findings as the studied nurses' source of information were not the in-service training, but 33.1% stated that their source was drug reference handbook, 19.8% of them take information from the pharmacist, and 19.5% depending on a combination of pharmacist, non-pharmacist and drug reference handbook. Unavailability of a computerized alert system and inconsistent internet access might be the reason why workshops, seminars, and lectures were the most cited source of information in the current study.

The current study finding is contradicted by a study done in the US revealed that the majority of prescribing nurses, 40.3% consulted computerized alert systems *(Carithers, 2011).* Furthermore, a study was done in Uganda also reported that freely available on-line medicine information tool was used to detect and manage potential DDIs *(Lubinga & Uwiduhaye 2011). Karahan et al. (2015)*, reported that 92.3% of nurses had information from in-service education. In a study conducted in Iran, most of the participants used software on mobile phones or tablets, and the internet was the most commonly used reference *(Nabovati et al., 2017).* A similar study conducted in Slovenia showed that they used the most popular software which was Micromedex® Drug-Reax *(Zheng et al., 2017). El Lassy and Ouda (2019)* reported that more than half of the information sources regarding DFIs were from the formal educational background; around one third got their information from networks and websites and more than one-quarter from the doctors.

Analysis of the nurses' history of encountering DDIs and DFIs reveals that more than half of the nurses came across patients who experienced either DDIs or DFIs. More than one-third of them encountered DDIs and DFIs twice, more than one quarter encountered it once, and one quarter encountered it several times. Half of the studied nurses reported familiarity with the standards of hospital treatment guidelines; half of them were somewhat familiar. These findings reflect the prevalence of DDIs in the clinical setting.

These findings are nearly similar to *Karahan et al. (2015)*, who reported that around half of the responders (40%) encountered drug interactions, and 59.1% sometimes

encountered DDIs, among them 22.6% encountered DDIs in last year. Also, 27.8% of nurses explored drug reactions with drinks, herbal 24.3%. *Endal et al. (2019)* also reported that more than half of the responders (59.1%) encountered drug interactions. The majority of respondents (66.6%) are familiar with the standard treatment guideline of the hospital.

These findings are inconsistent with *Enwerem et al. (2017),* who reported that most of the participated nurses did not observe adverse reactions due to FDIs during their clinical practice, and only 28% of the study participants had recorded FDIs during their clinical practice.

The most observed symptoms for DDIs and DFIs in the current study were nausea and vomiting observed by around fifty percent of the nurses who encountered that event. More than two-fifths of them observed dysrhythmias, more than one-third observe dizziness, around one quarter observed hypotension, about one fifth observed changes in blood pressure among the adverse outcomes of drug-drug or drug-food interactions. This finding reflecting the seriousness of the studied phenomena. *Karahan et al., (2015)* reported that the studied nurses observed nausea-vomiting (70.4%), dizziness (40%), heart rhythm problems and sudden changes in blood pressure in 28.7%, toxicity (35.7%), and headache (34.8%) due to drug interactions in the cancer patient.

The studied nurses' awareness reveals that around half of them did not know about the drug-drug interactions of the studied pairs of drugs that are frequently used in clinical practice such as Carbamazepine and Clarithromycin, Warfarin and Co-trimoxazole, and Digoxin and Sildenafil. This finding may be related to that around two-thirds of the studied nurses did not receive training other than that in their basic education regarding DDI and DFIs. This training may also lack focusing on DDIs and DFIs. Work overload and prolonged work hours may participate in the low nurses' awareness as more than half of the nurses working in emergency medicine, and around one-third of nurses spend between 31-40 hours in hospital per week, and around one-third of them spend more than 41-50 hours per week. More than half of the studied nurses administer between 10-20 prescriptions per day. The qualification of the studied nurses may contribute to poor awareness as half of them had a technical nursing diploma.

This result agrees with *Karahan et al. (2015), Elangovan et al. (2017),* who stated that nurses encountered drug-drug interactions and drug-food interactions more often than other interactions related to Warfarin, Captopril, and anti-inflammatory agents. Other studies added that antihypertensive and long-term corticosteroids raised the risks for potential drug-drug interactions, which is similar to the current study results that more than half of the studied nurses did not know about the interaction between Warfarin and Fluconazole, Digoxin and Clarithromycin, Digoxin and Verapamil, and Atenolol with Ranitidine.

These findings are supported by *Endal et al. (2019),* who reported that the percentage of health care professionals who correctly classified the drug pairs ranged from 10.6% for the drug pair Digoxin and Sildenafil to 43.7% for the drug pair Digoxin and Verapamil. Most of the participant's responses to the ten drug pairs were incorrect. On the other way, a study conducted in Saudi Arabia reported that about 92.2% of healthcare professionals correctly classified Warfarin interactions with Aspirin and 4.4% for Warfarin and Fluoxetine. This discrepancy might be due to the difference in knowledge assessment tools *(Al-Arifi et al., 2016).*

Near half of the studied nurses had a low total awareness regarding the DDIs. This finding may be referred that the nurses may not perceive the DDIs is a common phenomenon, or not significantly observed as adverse patients' outcomes. *Turabian (2019)* reported the same explanation in a study entitled "Approach to the epidemiology of drug interactions in primary health care." The study mentioned that there is an underestimation of the importance of DDIs. Thus, it can be thought that DDIs are not a significant problem. This result was also evidenced in the current study, as less than half of the studied nurses agreed about the risk of drug-drug and drug-food interactions are high.

These findings are supported by *Grizzle et al. (2007)*, who reported that health care professionals could not often identify and recall potential DDIs. *Gilligan et al. (2011); Ko et al. (2013)* reported a lower potential DDIs knowledge among nurse professionals. *Endal et al. (2019)* reported only 24.29% correct responses regarding DDI among the studied participants. Similar findings were reported by studies conducted in the University of Arizona, Iran, and general hospital of Addis Ababa, which reported correct responses among 42.7%, 41% and 33.3% of the studied nurses respectively *(Ko et al., 2013; Nabovati et al., 2017; Moges, 2013).* The results of these study were similar to some studies that indicated that medication knowledge of nurses was not at the desired level, and nurses need more knowledge *(Hsaio et al., 2010).*

The nurses' awareness of DFIs reveals that less than half of the studied nurses did not know about the DFIs for frequently used drugs. Around half were not sure of DFIs between asthma drugs and caffeine or high fiber diet, about the DFIs between Cephalosporines and fruit juice or wine, and about the DFIs of Penicillamine and dairy products or iron-rich foods or supplements, with low total awareness of DFIs among near to three-quarters of the studied nurses.

This finding may be referred to as the inadequate in-service training that focuses on DFIs, work overload, and nurses' qualifications. Besides, the nurses in the current study did not mention that they use any type of computer information system or mobile application to help them being oriented with DDI or DFIs. *Karahan et al. (2015)* concluded in their study that the nurses need education about drug-food interaction, and they suggested performing training programs in regular periods to increase their perception toward drug-food interaction. *Moradi et al. (2016)* also reported a low mean score of DFIs related knowledge among nurses.

Moreover, only one-third of the nurses' participants reported correct knowledge regarding Levodopa and protein meal, around half of them answered correctly about

Tetracyclines and dairy products, antibiotics and citrus juices, less than one third answered correctly about the interaction between Digoxin and wheat bran *(Enwerem et al., 2017).*

On the contrary, less than half of the studied nurses were sure about the DFIs of antihypertensive, antiarrhythmic drugs and caffeine, two-fifths of them were sure about the DFIs between the cholesterol-lowering drugs and fatty foods. This finding may be referred that these drugs had standard precautions that usually reported by the nurses as a health teaching for these drugs.

The present study reveals a low total level of awareness regarding DFIs among three-fourths of the studied nurses. This reflecting and emphasizing that DFIs are not a point of concern among nurses or nurse trainer. *El Lassy and Ouda, (2019),* reported that about four-fifths of the studied nurses had poor knowledge level (less than 50% of the total score) regarding DFIs before implementing an educational program regarding DFIs in pediatric outpatients' clinics. The control group nurses also showed more than four-fifths of them had poor knowledge at the beginning of the study regarding DFIs. They have reported the same explanation of nurses' unsatisfactory level of awareness that they lack the time and knowledge of properly manage DFIs, heavy workloads, and insufficient training may contribute to this level of knowledge.

Regarding the nurses 'perception of drug safety regarding the DDI and DFIs. Less than half of the studied nurses agrees with the risk of drug-drug interaction is high, the importance for prescribers to learn about DDIs and DFIs, the information regarding the DDIs, and DFIs useful to the nurse in plan management. Also, they agree with the information regarding DDIs and DFIs is relevant to patient safety, and the nurse is likely to consider DDIs and DFIs as a part of their decision, with high total perception regarding the drug safety (DDI and DFIs) among two-thirds of the studied nurses. In contrast, around half of them still thought that it is the function of the pharmacist.

These results are congruent with *Enwerem et al. (2017),* who revealed that the overwhelming majority of the nurses agreed with the steps that should be taken to prevent FDIs. The participants agreed that before a drug is dispensed, the label and pamphlets in the container should be read, the directions for use, interactions, and precautions should be read. Also, *Endal et al. (2019)* illustrated that (44%) of participants agreed that the risk of drug-drug interactions is high while the majority of them (66.6%) agreed that it is important for healthcare professionals to learn about drug-drug interaction.

The current study revealed a statistically significant positive correlation between nurses' perception of drug safety and nurse awareness of DFIs, while there is a non-statistically association between the nurses' perception of drug safety and nurses' awareness of DDIs. This result is evidenced that as the high awareness with DFIs increased either through education or clinical experience, the drug safety might improve and vice versa. This explanation is supported by the current study findings as a highly statistically significant association was found between nurses' educational levels and perception, and awareness to DDIs and FDIs as the highest mean scores were for the bachelor degree nurses in both perception and awareness to FDIs while the highest mean score was for diploma nurses regarding DDIs.

On the same line, the current study emphasized a statistically significant association between training received and nurses' awareness of DDIs and DFIs with those who receive training had the highest mean scores. Also, a statistically significant association was revealed between the type of training, and both perception of drug safety and the awareness of DDIs with those who received lecturing regarding the treatment interaction had the highest mean scores. This reflecting the importance of focused training on the awareness and perception of nurses regarding DDIs and DFIs.

This finding is consistent with *Carithers, (2011); Enwerem et al. (2017)*, who reported in a study about nurses' awareness of drug-food interaction that participants with associate degrees, scored worse than baccalaureate and graduate degree holders. From the open-ended question on how knowledge and awareness of FDI may be improved, most of the participants felt it is crucial to update knowledge of FDIs every six months through in-service training.

This finding is also congruent with *Alkhalidi et al. (2019),* who mentioned that the highest level of education of increased nurses' situational awareness and decreased task completion time. Also, information integration has the potential to decrease errors, increase nurses' productivity, and may allow nurses to react faster to a patient's clinical needs. *Endal et al. (2019),* also reported a statistically significant association between the health care professional perception and their knowledge regarding DDIs. *El Lassy and Ouda (2019)* reported a significant association between knowledge and qualifications (with Bachelor degree nurses had a better knowledge score).

This finding is inconsistent with *Kelly et al. (2010); Harrington et al. (2011); Ko et al. (2013),* who reported that nurses who used drug reference books as their usual drug-drug interaction information source or trained from the long period had a lower mean drug-drug interaction information score.

Also, a highly statistically significant association was demonstrated between the practice setting, and the awareness of DDIs as the nurses working in a governmental hospital had a higher mean score. This finding might be explained as the nurses in the governmental hospital are exposed to a high flow of patients with different medical diagnoses and polypharmacy. A statistically significant association was found between the area of specialization, and both perception and awareness of DDIs and DFIs as nurses in the renal department and emergency surgery had the highest mean scores of perception of drug safety.

In contrast, the nurses in internal medicine, chest, and heart surgery represented the highest mean score of awareness to DDIs, and the nurses in internal medicine and emergency surgery had the highest mean scores of awareness of DFIs. This finding may be due to those nurses

in renal, emergency surgery, internal medicine, and chest and heart surgery are exposed to numerous amounts of variable polypharmacy, hence various drug-food precautions. This result is in line with the finding by *Ko et al. (2013).*

Besides, there was a statistically significant association between the average number of patients cared for by the nurse per day and the nurses' perception of drug safety with the nurses who cared for less than 15 patients per day had the highest mean score. A statistically significant association was revealed between hours spent by the nurses in the hospital, and their awareness of DDIs and DFIs with the nurses who spend between 20-30 hours had the highest mean. This finding might evidence that the nurses who cared for a reasonable number of patients and working hours allowed them to observe patients more meticulously, and the increased workload can hinder proper patient care. These results are in line with *Warholak (2011); Enwerem and Okunji (2015); Alkhalidi et al. (2019),* who reported that the number of hours spent in the hospital has a positive effect on the awareness of nurses to drug-drug interaction. This finding is also evidenced by the current study as more than half of them care for fifteen to twenty patients per day, about two-thirds of them spend between thirty-one and forty hours in hospital per week and around one third spend between forty-one and fifty hours per week. Besides, more than half of them administer between ten to twenty prescriptions per day.

Also, A highly statistically significant association was revealed between the average number of prescriptions administered per day and DFIs with the nurses who gave the highest number of prescriptions had the highest mean score of FDIs' awareness. This finding reflects that the high nurses' exposure could empower her clinical experience regarding the DDIs and DFIs. This finding is similar to *Endal et al. (2019)* finding, who showed that work experience, familiarity to the standard treatment guideline, source of information, showed significant association to the healthcare professionals' DDIs knowledge.

7. Conclusion

The findings of the current study revealed that around two-thirds of studied nurses did not receive training on DDIs or DFIs other than that in their formal education. More than half of the nurses came across patients who experienced either DDIs or DFIs. Regarding awareness, around half of them did not aware of the drug-drug interactions of the studied pairs of drugs that are frequently used in the clinical practice. Less than half of the studied nurses did not know about the DFIs for frequently used drugs with a low total level of awareness regarding DFIs among three-fourths of the studied nurses.

Regarding nurses' perception of drug safety, around half of the studied nurses agree with the risk of drug-drug interaction is high, the importance for prescribers to learn about DDIs and DFIs, and the information regarding the DDIs and DFIs useful to the nurse in plan management. The current study revealed a statistically significant positive association between nurses' perception of drug safety and nurse awareness of DFIs. The study also shows a statistically significant difference between training received and nurses' awareness of DDIs and DFIs. Besides, there was a statistically significant difference between the average number of patients cared for by the nurse per day and the nurses' perception of drug safety. A statistically significant difference was revealed between hours spent by the nurses in the hospital and their awareness of DDIs and DFIs.

8. Recommendations

Based on the results of the study, implementation and dissemination of comprehensive, systematic, and continuous educational programs in order to enhance the knowledge, practices, and perceptions of nurses on DDIs and DFIs was recommended.

Medication reviews should be undertaken regularly, particularly in older frail people with polypharmacy that should be evaluated and monitored for the positive impact on the medication use system and improvement of quality of patient care.

Different strategies should be applied to assist prescribers in identifying potential DDIs, providing educational interventions, facilitating access to DDI information sources, applying computerized alerting systems, and delivering performance feedback is among the most commonly recommended strategies.

Other information sources such as smartphone applications that provide drug-drug interaction information that is up to date, easy to use, and portable than drug reference books or training should be used. Therefore, those nurses who relied on these information sources can seek drug-drug interaction information at any time.

A recommendation for further researches to study the association between patient numbers cared for by a single nurse, working hours, years of experience, a different source of information, and nurses' awareness of DDIs and DFIs.

9. References

Ahmad, A., Khan, M.U., Haque, I., Ivan, R., Dasar, R., Revanker, M., Pravina, A., & Kuriakose, S. (2015). Evaluation of potential drug-drug interactions in general medicine ward of teaching hospital in Southern India. *Journal of Clinical and Diagnostic Research*, *9*(2), FC10-FC13. https://doi.org/10.7860/JCDR/2015/11264.5608

Agency for Health Care Research and Quality Patient Safety Network. (2007). Patient safety. [Accessed October 20, 2007]. http://psnet.ahrq.gov/glossary.aspx#P.

Alkhalidi, D., & Jamshed, S. H. (2019). General public views, attitudes, and experiences toward drug safety in Dubai, United Arab Emirates: A qualitative Approach, Pharmacy, *7*(1), 19. https://doi.org/10.3390/pharmacy7010019

Al-Arifi, M. N., Wajid, S., Al-Manie, N. K., Al-Saker, F. M., Babelgaith, S. D., Asiri, Y. A., & Sales, I. (2016). Evaluation of knowledge of Health care professionals on warfarin

interactions with drug and herb medicinal in Central Saudi Arabia. *Pakistan journal of medical sciences, 32(1),* 229–233. https://doi.org/10.12669/pjms.321.8902

Ali, H., Zafar, F., Shaukat, A., Alam, S., Ali, U., Shareef, H., Mallick, N., Shafiq, Y., Hasnain, H., Naveed, S., & Naqvi, G. R. (2017). Narrow therapeutic index drugs; perception, practice, facts and knowledge of healthcare professionals in identification and management of interactions. *Professional Medical Journal*, *24*(4), 596-606. https://doi.org/10.17957/TPMJ/17.3746

Amirthalingam, S., & Vaidhun, B. H. (2010). Drug interactions: A view of doctors. *Annals of Biological Research*,*1*(1), 61-69.

Arnold, R. J. G., Tang, J., Schrecker, J., &Hild, C. (2018). Impact of definitive drug-drug interaction testing on medication management and patient care. *Drug-Real World Outcomes*, *5,* 217-224. https://doi.org/10.1007/s40801-018-0143-z

Attari, A., Aminoroaia, M., &Maracy, M. (2017). Efficacy of purposeful educational workshop of medical and nonmedical interventions based on needs assessments in nurses. *Journal of Education and Health Promotion,* 6, 18. https://doi.org/10.4103/2277-9531.204745

Bertoli, R., Bissigb, M., Caronzoloc, D., Odoricod, M., Pons, M., &Bernasconi, E. (2010). Assessment of potential drug-drug interactions at hospital discharge. Swiss Medical Weekly March. Available from http://smw.ch/docs/PdfContent/smw12979.pdf

Bushra, R., Aslam, N., &Yar Khan, A. (2011). Food-Drug Interactions. *OmanMedical Journal, 26*(2), 77-83. https://doi.org/10.5001/omj.2011.21

Carithers, C. (2011). A study of nurse practitioner characteristics and knowledge of drug-drug interactions. University of Arizona; Doctor of Nursing Thesis. http://www.nursing.arizona.edu/Library/Carithers _Cathrin_Practice_Inquiry.pdf

Cherry, K., & Gans, S. (2019). How does the cross-sectional research methods work? Student resources. Very well mind. https://www.verywellmind.com/what-is-a-cross-sectional-study-2794978#how-and-when-cross-sectional-studies-are-used

Dechanont, S., Maphanta, S., Butthum, B., & Kongkaew, C. (2014). Hospital admissions/ visits associated with drug-drug interactions: A systematic review and meta-analysis. *Pharmaco epidemiol Drug Saf*, 23, 489–97. https://doi.org/10.1002/pds.3592

El Lassy, R. B. M., & Ouda, M. M. (2019). The Effect of food-drug interactions educational program on knowledge and practices of nurses working at the pediatric outpatients' clinics in El-Beheira General Hospitals. *Journal of Nursing and Health Science*, 8(4), 34-48. https://doi.org/10.9790/1959-0804013448

Elangovan,V., Rajaraman, S., & Basumalik, B. (2017). Awareness and perception about cancer among the public in Chennai, India, *Journal of global oncology, 3*(5), 469–479. https://doi.org/10.1200/JGO.2016.006502

Elhada, A. H. A., AlRawashdeh, H., Madi, L., & Ahmed, A. (2018). Increasing nurses' awareness of drug Interactions. Conference: 4th Qatar International Pharmacy Conference. Research gate. https://www.researchgate.net/publication/327559364

Endal, B., Getnet, D., & Gebrie, D. (2019). Healthcare professionals' awareness of drug-drug interaction in Ayder comprehensive specialized hospital Mekelle, Ethiopia. *International Journal of Hospital Pharmacy*, *4*(32), 1-9.

Enwerem, N., & Okunji, P. (2017). Knowledge of food and drug interactions among nurses: Assessment strategy for continuing education. *International Journal of Higher Education*, 6, 122-130. https://doi.org/10.5430/ijhe.v6n1p122

Enwerem, N. M., Okunji, P., & Johnson, A. (2017). Food-Drug Interactions: Implications for Nursing Practice. *Nursing & Healthcare International Journal*, 1(1), 000102.

Enwerem, N. M., & Okunji, P. (2015). Knowledge, attitudes, and awareness of food and drug interactions among nurses with different levels of experience. *IJN, 2*(1). https://doi.org/10.15640/ijn.v2n1a1

Faria, L., & Cassiani, S. (2011). Medication interaction: Knowledge of nurses in intensive care units. *Acta paul. Enferm, 24*(2), 264-270. https://doi.org/10.1590/S0103-21002011000200017

Food and Drug Administration. (2009). Preventable adverse drug reactions: A focus on drug interactions; 2009. Available from: http://www.fda.gov/drugs/developmentapprovalprocess/ developmentresources/druginteractionslabeling/ucm110632. htm#ADRs:%20Prevalence%20and%20 Incidence.

Frandsen, G., & Pennington, S. S. (2014). *Basic concepts and processes In İyigün E, Taştan S, editors. Abrams's Clinical Medicine Treatment: Practice of Rational Drug for Nurses.* 10th ed. Ankara, Turkish: Akademisyen Medicine Book, p. 25.

Gebretsadik, Z., Gebrehans, M., Getnet, D., Gebrie, D., Alema, T., &Belay, Y. B. (2017). Assessment of drug-drug interaction in Ayder comprehensive specialized hospital, Mekelle, Northern Ethiopia: A retrospective study. *BioMed Research International*. https://doi.org/10.1155/2017/9792363

Gilligan, A. M., Warholak, T. L., Murphy, J. E., Hines, L. E., & Malone, D. C. (2011). Pharmacy students' retention of knowledge of drug-drug interactions. *American journal of pharmaceutical education*, *75*(6), 110. https://doi.org/10.5688/ajpe756110

Grizzle, A. J., Mahmood, M. H., Ko, Y., Murphy, J. E., Armstrong, E. P., Skrepnek, G. H., Jones, W. N., Schepers, G. P., Nichol, W. P., Houranieh, A., Dare, D. C., Hoey, C. T., & Malone, D. C. (2007). Reasons provided by prescribers when overriding drug-drug interaction alerts. *Managed Care, 13*(10), 573-580.

Guthrie, B., Makubate, B., Hernandez-Santiago, V., & Dreischulte, T. (2015). The rising tide of polypharmacy and drug-drug interactions: Population database analysis 1995-

2010. *BMC Med*, *13*, 74. https://doi.org/10.1186/s12916-015-0322-7.

Hsaio, G. Y., Chen, I. J., Yu, S., Wei, I. L., Fang, Y. Y., &Tang, F. I. (2010). Nurses' knowledge of high-alert medications: Instrument development and validation. *J Adv Nurs*, *66*,177-90. https://doi.org/1010.1111/j.1365-2648.2009.05164.x.

Harrington, A. R., Warholak, T. L., Hines, L. E., Taylor, A. M., Sherrill, D., &Malone, D.C. (2011). Healthcare professional students' knowledge of drug-drug interactions. *American journal of pharmaceutical education*, *75*(10), 199. https://doi.org/10.5688/ajpe7510199

Institute of Medicine Recommendations (2010). The future of nursing leading change, advancing health advising the nation/improving health. https://www.ncbi.nlm.nih.gov/pubmed/24983041

Karahan, A., Isik, S., Kav, S., & Abbasoglu, A. (2015). Oncology nurses' awareness of drug interactions. *Asia Pacific Journal of Oncology Nursing. 2, 271-5.* https://doi.org/10.4103/2347-5625.164998

Kaufman, G. (2016). Polypharmacy: The challenge for nurses. *Nursing Standards*, *30*(39), 52-60. https://doi.org/10.7748/ns.30.39.52.s45

Kelly, C. M., Juurlink, D. N., Gomes, T., Duong-Hua, M., Pritchard, K. I. & Austin, P.C., & Paszat, L. F. (2010). Selective serotonin reuptake inhibitors, and breast cancer mortality in women receiving tamoxifen: a population-based cohort study, *BMJ (Clinical research ed.).* 340, c693. https://doi.org/10.1136/bmj.c693

Khan, H. M.S., But, H., & Shah, N. H. (2014). Exposure to potential drug-drug interactions in teaching hospital of South Punjab, Pakistan. *Value in Health*, *A323-A686* https://www.valueinhealthjournal.com/article/S1098-3015(14)02988-X/pdf

Ko, Y., Malone, D.C., Skrepnek, G.H., Armstrong, E.P., Murphy, J.E., Abarca, J., Rehfeld, R. A., Reel, S. J., &Woosley, R. L. (2013). Prescribers' knowledge of and sources of information for potential drug-drug interactions: a postal survey of US prescribers', *Drug Safety, 31*(6), 525–536. https://doi.org/10.2165/00002018-200831060-00007

Kothari, N., & Ganguly, B. (2014). Potential drug-drug interactions among medications prescribed to hypertensive patients. *Journal of clinical and diagnostic research*, *8*(11). HC01-4. https://doi.org/10.7860/JCDR/2014/10032.5091.

Lubinga, S. J., & Uwiduhaye, E. (2011). Potential drug-drug interactions on in-patient medication prescriptions at Mbarara Regional Referral Hospital (MRRH) in western Uganda. *African Health Scince*, *11*(3), 501-02, and 499–507.

Moges, G. (2013). Assessment of physicians' awareness of drug-drug interaction and common source of information in the general hospital of Addis Ababa. Master's Thesis. Addis Ababa University. Available from: http://etd.aau.edu.et/bitstream/handle/12345678 9/1837/Getachew%20Moges.pdf?sequence=1&i sAllowed=y

Mohamed, S. M., Gad, Z. M., El-Nimr, N. A., & Abdel Razek, A. A. (2015). Prevalence and pattern of drug-drug interactions in the critical care units of a tertiary hospital in Alexandria, Egypt. Poster presentation. *International Journal of Epidemiology*, 44 (Suppl. 1). https://doi.org/10.4172/2167-1052.1000144

Moradi, Y., Rahmani, A. R., Gholipour, K. H., Mirzaie, R., Samadi, N., & Al-Sharaa, S. A. (2016). Nurses' pharmacology knowledge of food-drug interactions in Ayatollah Taleghani Hospital of Orumieh, Iran., *Journalof Chemical and Pharmaceutical Science, 9*(3), 1083-1087. https://www.researchgate.net/publication/309104607_Nurses'_pharmacology_knowledge_of_food-drug_interactions_in_Ayatollah_Taleghani_Hospital_of_Orumieh_Iran

Nabovati, E., Vakili-Arki, H., Taherzadeh, Z., Saberi, M. R., Abu-Hanna, A., & Eslami, S. (2017). A survey of attitude, practice, and knowledge regarding drug-drug interaction among medical residents in Iran. *Int J Clin pharm, 39*(3),560-568. https://doi.org/10.1007/s11096-017-0453-3

Ötles, S., & Senturk, A. (2014). Food and drug interactions: A general review. *Acta Sci. Pol., Technol. Aliment. 13*(1), 89-102. https://pubmed.ncbi.nlm.nih.gov/24583386/

Palleria, C., Di Paolo, A., Giofre, C., Caglioti, C., Leuzzi, G., & Siniscalchi, A. (2013). Pharmacokinetic drug-drug interaction and their implication in clinical management. *J Res Med Sci, 18, 601-610.* https://pubmed.ncbi.nlm.nih.gov/24516494/

Piscitelli, S., Rodvold, K., & Pai, M. (2011). *Drug Interactions in Infectious Diseases.* Third Edition. Springer New York Dordrecht Heidelberg London. Humana Press. www.springer.com.

Roblek, T., Vaupotic, T., Mrhar, A., &Lainscak, M. (2015). Drug-drug interaction software in clinical practice: A systematic review. *European Journal of Clinical Pharmacology*, *71*(2), 131–142. https://doi.org/10.1007/s00228-014-1786-7

Schrecker, J., Puet, B., Hild, C., & Schwope, D. M. (2018). Characterization of drug-drug interactions in patients whose substance intake was objectively identified by detection in urine. *Expert Opinion on Drug Metabolism & Toxicology, 14*(9), 973-978. https://doi.org/10.1080/17425255.2018.1509953

Simonsen, B., Daehlin, G., Johansson, I., & Farup, P. (2014). Differences in medication knowledge and risk of errors between graduating nursing students and working registered nurses: Comparative study. *BMC Health Serv Res*, *14*, 580-591. https://doi.org/10.1186/s12913-014-0580-7

Sulosaari, V., Suhonen, R., & Leino-Kilpi, H. (2010). An integrative review of the literature on registered nurses' medication competence. *Journal of Clinical Nursing*, *20*, 464–478. https://doi.org/10.1111/j.1365-2702.2010.03228.x

Thanacoody, H. K. R. (2012). Drug interactions. In: Walker R, Whittlesea C (Eds). *Clinical Pharmacy and Therapeutics.* 5th ed. London: Elsevier. Pp. 50-61.

Turabian, J. L. (2019). Approach to the epidemiology of drug interactions in primary health care. The visible part of a great dangerous iceberg growing rapidly. *Epidemiology International Journal*, *3*(2), 1-10, https://doi.org/10.23880/eij-16000126

Unroe, K. T., Pfeiffenberger, T., Riegelhaupt, S., Jastrzembski, J., Lokhnygina, Y., & Colon-Emeric, C. (2010). Inpatient medication reconciliation at admission and discharge: A retrospective cohort study of age and other risk factors for medication discrepancies. *The American Journal of Geriatric Pharmacotherapy, 8(2)*, 115-126. https://doi.org/10.1016/j.amjopharm.2010.04.002

Warholak, T. L., Hines, L. E., Song, M. C., Gessay, A., Menke, J. M., Sherrill, D., Reel, S., Murphy, J. E. & Malone, D. C. (2011). Medical, nursing, and pharmacy students' ability to recognize potential drug-drug interactions: a comparison of healthcare professional students, *Journal of the American Academy of Nurse Practitioners, 23*(4), 216–221.

Zheng, W. Y., Richardson, L. C., Li, L., Day, R. O., Westbrook, J. I., & Baysari, M. T. (2017). Drug-drug interactions and their harmful effects in hospitalized patients: systemic review and meta-analysis. *Eur J Clin Pharmacol*. *74*(1), 15-27 https://doi.org/10.1007/s00228-017-2357-5.