# NARROW THERAPEUTIC INDEX DRUGS;
## PERCEPTION, PRACTICE, FACTS AND KNOWLEDGE OF HEALTHCARE PROFESSIONALS IN IDENTIFICATION AND MANAGEMENT OF INTERACTIONS

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**Article received on:**
28/11/2016
**Accepted for publication:**
02/02/2017
**Received after proof reading:**
06/04/2017

**ABSTRACT… Introduction:** There are several clinically significant outcomes of drug-drug interactions (DDIs) which have been classified as one of the serious forms of adverse drug reactions that may lead to prolongation of hospital stays along with severe cases of mortality and morbidities. It may cause due to the selection of two or more interacting drugs to be prescribed to patient. **Objectives:** Therefore it is indispensable to attain a collective level of therapeutic decision making so that any potential DDIs can be minimized that ultimately turn out to be safe and beneficial to patient. **Study Design:** The current study is based upon surveys to evaluate utilization of medications that have a narrow therapeutic range with high incidence to develop DDIs and to access the knowledge, attitude as well as practice of using such drug products in relation to these facts, though very few such studies have been identified, yet the relevant data is insufficient locally. The study design was selected to be qualitative and cross sectional. **Period:** January 2016 till August 2016 in Karachi, Pakistan. **Settings:** The questionnaire was well constructed for physicians, pharmacists as well as nurses who were selected as the participant of the study and a former consent from the respondents was obtained. **Method:** Coefficient of spearman correlation & Cronbach's α values were calculated in order to validate the questionnaire (α = 0.927 and p = 0.918). The information based on practice along with demographics of study participant was included as first segment of questionnaire while their knowledge regarding drug interactions was included as second part. Mean scores were calculated and responses were analysed by ANOVA in relation to the knowledge of members relating to drug interactions of vancomycin, warfarin and valproic acid. **Results:** Mean scores of perception were found in order of 1.590.16, 1.549.02 and 2.020.83 for physicians, pharmacists and nurses. No significant differences were observed between physicians and pharmacists cohorts in identifying the drug interactions whereas noteworthy variations were observed in the group of nurses (p < 0.05). **Conclusion:** Such investigations are vital in their prospect to highlight the importance for the design, implementation and monitoring of an effectual tool for the guidance of various healthcare members involved in identification and management of DDIs. Furthermore, results also signify the need of sophisticated support systems for valuable clinical judgments.

**Key words:** Drug- Drug Interactions, Practice, Knowledge, Mean Score, Pharmacist, Physician, Nurses.

## INTRODUCTION

Every year thousands of drugs are being introduced in the market, which results in numerous new interactions between medications reported annually. Consequently, to avoid probable interactions of drugs doctors cannot just depend on their memory alone. In individuals with minor illness drug interactions may not be of great clinical importance but may results in severe clinical conditions, morbidities and death in individuals with ailments of chronic nature.[1]

For better outcome of treatment it is very important to stick to prescribed medication however it is a challenge for health professionals to educate and counsel an illiterate patient.[2] Due to poly pharmacy during treatment the patients at high risk are particularly the elderly, critical

care patients and those undergoing surgical procedures. It is reported by the researchers that about 80 % of elderly patients constantly taking prescribed and none prescribed medications simultaneously.[3] Due to diverse age-related physiologic changes, high risk for a variety of complex illness associated with aging, and the consequently over use of medication, elderly patients are more susceptible to drug interactions in comparison to younger individuals.[4]

The bioavailability, pharmacodynamics, pharmacokinetics and therapeutic efficiency of the medication might be influenced by interactions between foods and drugs because dose, age, size and state of health care the factors involved in food and drug interaction. Likewise multiple drugs in prescriptions, dietary appendages, poor adherence to drugs, deprived patient knowledge and counselling gaps are the prime reasons for reduce therapeutic outcomes.[5-6] To offer best patient care or counselling and to minimise the adverse effect events it is considerably important to have proficient and skilled healthcare professionals in their respective area of expertise.[7] Due to the fact that therapeutic improvement depends on healthcare proficiencies, formerly many researches has been conducted around the world to figure out the effect of all the factors involved in drug interaction and their therapeutic outcomes.[8-10] Patients that are prescribed medication with narrow therapeutic range need to be monitored closely for prime care, treatment and for minimising any possible drug-food or drug-drug interactions. So in these circumstances the healthcare professionals play important role.[11] It is vital for healthcare professionals to be aware of possible drug-drug interactions (DDIs) to minimise the risk of any viable DDIs and associated adverse effects. It has been observed only small number of literatures foresight the evidence about the physician's explanation on DDIs knowledge.

## OBJECT OF STUDY
The current research was designed to conclude healthcare professional's acquaintance utilization of an array of information origin, and to study the analytical factors that might be related in this

perspective. In present study an observation regarding utilization of drugs within the narrow therapeutic range and associated drug interactions with reference to professional awareness and expertise were monitored.

## MATERIAL AND METHODS
### Study design
The present study was conducted to explicate the approach (attitude), awareness and acquaintance/information of different healthcare professionals associated to drug interaction knowledge. In order to elicit the relevant information a questionnaire (data collection form) was designed to find out the practices, knowledge and awareness of different members of healthcare team including doctors, nurses and pharmacist. Questions were selected from reported sources of literature with reference to frequent and definite types of drug interactions.[12-14] A panel of expert (physician, pharmacologist and pharmacists with relevant clinical experience) was formulated to evaluate the relevance and strength of questionnaire. Few of the questions were judged irrelevant during the phase of review with respect to customary (routine) clinical practices and hence removed from the list, while some question were also modified in order develop the meticulousness and clarity. Participants consents were collected prior the study. Coefficient of spearman correlation & Cronbach's α values were calculated in order to validate the questionnaire ($\alpha = 0.927$ and $p = 0.918$).

### Data collection
The final questionnaire was subsequently composed of two portions. Initial segment included the related questions (N=7) to determine the demographic facts along with practice based information. Demographic profile of respondents was determined with respect to gender, professional experience in related field and age. Whereas, the second part of questionnaire was formulated to reveal the skills and knowledge of respondents in the area of drug interaction. This portion of questionnaire was divided into three segments to elucidate the specific level of information for interactions of valproic acid, warfarin and vancomycin with diverse groups of medications. Customary practices in relation to drug interaction identification and

management were examined using a set of close ended questions. Simultaneously data was also collected regarding the application and utilization of a variety of sources to obtain the relevant knowledge and proofs concerning drug interactions. Perceptions toward DI in various cohorts were calculated using mean scores approach and likert scale was taken into account for the observation of the perception/awareness of study participants towards DDIs.

## Sample size

A convenient and random sample (N=100) of pharmacist, physicians and nurses was included in this survey from various practicing areas (healthcare settings) from Karachi city, Pakistan. Prior consents were taken from individual participant. Questionnaire were distributed and collected by the investigators and few trained volunteers. Return response of forms was 61% for physicians (N=61), 50% each for nurses and pharmacists (N=50).

## Inclusion and Exclusion criteria

All participants which were involved in tertiary care practice area were incorporated in this investigation, whilst professionals involved in primary care setup were not integrated in this study as recourse allocation in both set up is widely different.

## Data analysis

SPSS 20 (SPSS Inc) was used to analyze the results. Responses of particular groups were evaluated using analysis of variance (ANOVA) approach regarding altitude of respective knowledge of different interactions of warfarin with statins, antacids (sucralfate and cimetidine), vitamin C and E, propranolol, aspirin, atenolol and cholestyramine. Moreover, level of knowledge for vancomycin and valproic acid interactions with diverse groups of medicines were also estimated in the similar manner taking p values < 0.05 (noteworthy significant with 5% limit of bound of error).

## RESULTS

Drug interactions can occur with other prescribed drugs as well as also with the use of diverse herbal products, foods and dietary supplements.[15] It is observed that Patients taking approximately 3 drugs may experience drug interactions range from 3 to 5%, which may rise to 20% with increase in number of medication up to 20.[2,16] In present investigation the demographic profile of approximately 161 health care participants such as (physicians, pharmacists and nursing staff) were summarized in Table-I with their mean age of 29 to 30 years and 35 years correspondingly. The number of male doctors 62%, pharmacists 60% and 64% lady nursing staff were the dominant respondents. Almost 74% of nursing workforce and 46% of health practitioners had less work exposure of 1-3 years in their related fields in contrast to 40% of pharmacists with 4-6 years professional skills. However, only 2% doctors found to have 19 to 21 years of practical experience shown by Figure-1. Moreover, Figure-2 and 3 represented the percentage of respondents who correctly answered the interactions of warfarin, valproic acid and vancomycin against different drugs. Although it is very obvious that doctors and pharmacists encompass significant knowledge but nurses have lack of awareness about drug-drug interaction (DDIs). Doctors ranked high to have drug interaction knowledge particularly for antibiotics, vitamins and cholestyramine, isoniazid, carbapenems and theophylline where as pharmacists have shown significant drug information about antacids, β- blockers, statins, colistin, furosemide, aminoglycoside and tetracyclins. Table-II depicted the practising aspects of professionals for identification of drug interaction (DIs) and various sources utilized to evaluate the potentials for prescription handling. Just 2% nurses availed the internet facility while 39% doctors shown to have excellent memory and taken guidance from books and 34% of pharmacists had high quality recalled ability as well as get information concerning DIs from sources such as web searching/internet/softwares and books etc. Replies of study participants were categorized as correct, incorrect and don't know patterns for scoring DIs between anticoagulants and various drugs presented in Table-III. The participants got a credit that manifestly recognizes the exact potential of DIs. A response

of not sure termed as incorrect and answer with poor knowledge specified an option as don't know. Many literatures were reported to facilitate DIs recognition and exploitation of computer aided tools for such activities in earlier period.[17-18] Several open and close ended questions were summarized in Table-II(a). According to Table-III, pharmacists and doctors responded well as corrected answer regarding DIs of cardiovascular and other drugs with anticoagulants. In present study, majority of doctors were well aware about DIs with cholestyramine and statins but around 69% and 62% of doctors had no idea about interaction of warfarin with aspirin and propranolol. Similarly 64% of nurses specified incorrect answer for aspirin DIs although 35% of pharmacists clearly identified such potential interactions. Furthermore, most of pharmacists found to have substantial concern of anticoagulant interactions with propranolol, atenolol and antacids than with statins and cholestyramine. Despite this fact, 33% nurses also had better knowing for unfavourable interactions of propranolol comparative to lesser awareness for statins 11% and antacids 18% as well. However, number of pharmacists was significantly lesser who exactly don't know the DIs of cardiovascular medicines with anticoagulant. In addition to this, the responses obtained from allied health care experts in Table-IV may differ in case of sound effects of various drugs on valproic acid and vancomycin. Numerous investigators have confirmed the task of healthcare participants and their combined efforts in detection and avoidance of drug-drug interactions.[19-20]
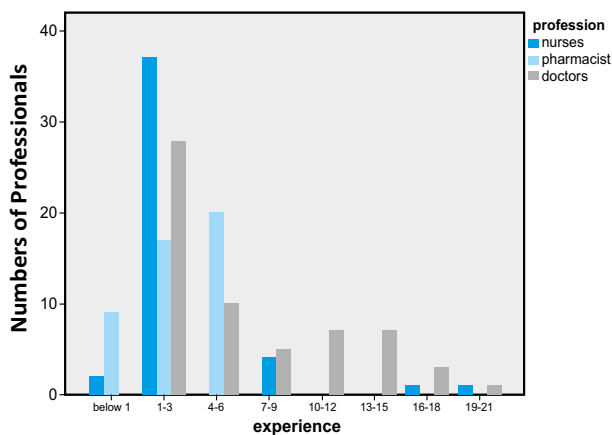


**Figure-1. Range of experience vs. Number of study participants**
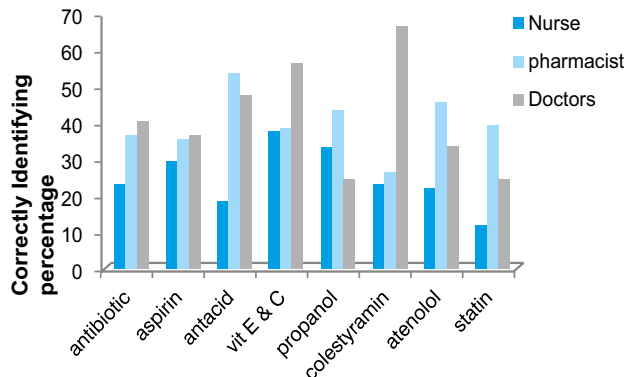


**Figure-2. Percent of respondents correctly answered for warfarin interaction with selected drugs**
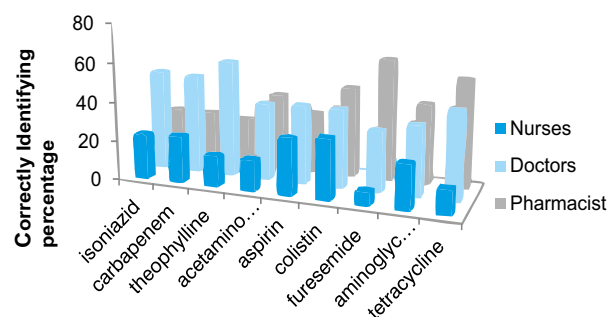


**Figure-3. Percent of Respondents Correctly Answered for Valproic Acid and Vancomycin Interaction with Selected Drugs**

| Particulars | Pharmacists | Doctors | Nurses |
|---|---|---|---|
| **Age** | | | |
| 20-29 | 39(78%) | 31(51%) | 43(86%) |
| 30-39 | 11(22%) | 22(36%) | 5(10%) |
| 40-49 | - | 8(13%) | 1(2%) |
| 50-59 | - | - | 1(2%) |
| Mean ± SD | 30 ± 4.6 | 35 ± 7.8 | 29 ± 6.7 |
| **Gender** | | | |
| Male | 30(60%) | 38(62%) | 18(36%) |
| Female | 20(40%) | 23(38%) | 32(64%) |
| **Years of Experience** | | | |
| Below 1 Year | 9(18%) | - | 2(4%) |
| 1-3 years | 17(34%) | 28(46%) | 37(74%) |
| 4-6 years | 20(40%) | 10(16%) | 9(18%) |
| 7-9 years | 3(6%) | 5(8%) | - |
| 10-12 years | 1(2%) | 7(11%) | - |
| 13-15 years | - | 7(11%) | - |
| 16-18 years | - | 3(5%) | 1(2%) |
| 19-21 years | - | 1(2%) | 1(2%) |
| **Table-I. Demographic profiles of study participants** | | | |

| Sources | Pharmacists | Doctors | Nurses |
|---|---|---|---|
| Memory | 5(10%) | 8(13%) | 32(64%) |
| Books | 4(8%) | - | 2(4%) |
| Software | 4(8%) | - | - |
| Web/Internet | 5(10%) | 6(10%) | 1(2%) |
| Memory + Books | - | 24(39%) | 15(30%) |
| Memory + Software | 5(10%) | 14(23%) | - |
| Memory + Books + Software | 7(14%) | 6(10%) | - |
| Memory + Books + Website | 3(6%) | 3(5%) | - |
| Memory + Books + Software + Website | 17(34%) | - | - |

**Table-II. Sources To Estimate The Potential Drug –Drug Interaction When Reading \Writing\Handling The Prescription**

| |
|---|
| Q. Demographic information related to age, gender and year of experience |
| Q. Do you consider drug – drug interaction to be an important Aspect when you are writing\reading a prescription |
| Q. How would you evaluate a potential DRUG –DRUG INTERACTION when writing\reading a Prescription? |
| Q. Do you think Therapeutic Drug Monitoring of narrow therapeutic index is an important element of patient's course of therapy? |
| Q. In your practice, have you come across any serious drug – drug interaction? |
| Q. How do antibiotics, aspirin, antacids, statins, vitamin C& E and different cardiovascular drugs affect the anticoagulant therapy of Warfarin? |
| Q. How do isoniazid, carbapenems, antacids, theophylline, acetaminophen and aspirin affect the plasma levels of Valproic Acid/Sodium Valproate? |
| Q. How do colistin, furosemide, aminoglycoside, tetracycline and theophylline affect the ototoxicity and nephrotoxicity of Vancomycin? |

**Table-II(a). Summary of questionnaire for healthcare professional**

Pertaining to the DIs of different therapeutic agents with valproic acid, pharmacists showed maximum record of accurate information with isoniazid 51%, carbapenems 50%, theophylline 59%, acetaminophen 65% and aspirin 40% to distinguish the DIs facts of doctors and nurses.

Tables-V&VI summarized the professional's responses information in terms of ANOVA and Chi-square for respective interacting moieties. Mean scores of perception calculated on likert based scale are summarized in Table-VII.

| Cardiovascular Drugs | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Profession | Atenolol | | | Cholestyramine | | | Propranolol | | | Propranolol | | |
| | Correct | Correct | Correct | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know |
| Nurses | 15 (22%) | 15 (22%) | 15 (22%) | 9 (23%) | 23 (29%) | 12 (26%) | 32 (33%) | 9 (30%) | 9 (26%) | 3 (11%) | 36 (40%) | 11 (25%) |
| Pharmacist | 30 (45%) | 30 (45%) | 30 (45%) | 9 (26%) | 36 (43%) | 5 (12%) | 42 (43%) | 4 (13%) | 4 (12%) | 11 (39%) | 32 (36%) | 7 (16%) |
| Doctors | 24 (33%) | 24 (33%) | 24 (33%) | 35 (66%) | 29 (34%) | 4 (10%) | 24 (48%) | 16 (26%) | 21 (62%) | 26 (65%) | 21 (24%) | 14 (43%) |
| Total | 69 | 69 | 69 | 53 | 84 | 39 | 98 | 29 | 34 | 40 | 89 | 32 |

| Other Drugs | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Profession | Antacid | | | Aspirin | | | Antibiotic | | | Vitamin E & C | | |
| | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know |
| Nurses | 9 (18%) | 34 (42%) | 7 (24%) | 40 (29%) | 7 (64%) | 3 (23%) | 23 (23%) | 23 (27%) | 4 (14%) | 22 (37%) | 16 (27%) | 12 (29%) |
| Pharmacist | 27 (53%) | 18 (22%) | 5 (17%) | 48 (35%) | 1 (9%) | 1 (8%) | 36 (35%) | 5 (33%) | 9 (32%) | 23 (38%) | 21 (36%) | 6 (14%) |
| Doctors | 29 (47%) | 15 (24%) | 17 (27%) | 49 (36%) | 3 (27%) | 9 (69%) | 40 (41%) | 6 (40%) | 15 (54%) | 15 (56%) | 22 (18%) | 24 (22%) |
| Total | 65 | 81 | 29 | 137 | 11 | 13 | 99 | 34 | 28 | 60 | 59 | 42 |

**Table-III. Responses of Individuals Regarding Effects of Cardiovascular and Other Drugs on Anticoagulants**

| Valproic Acid | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Profession** | **Theophylline** | | | **Carbapenems** | | | **Isoniazid** | | | **Aspirin** | | | **Acetaminophen** | | |
| | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know |
| Nurses | 9(16%) | 18(35%) | 23(40%) | 15(24%) | 19(38%) | 16(33%) | 18(23%) | 18(45%) | 14(33%) | 20(29%) | 11(26%) | 19(40%) | 7(16%) | 22(38%) | 21(35%) |
| Pharmacist | 29(59%) | 16(31%) | 5(8%) | 31(50%) | 15(30%) | 4(8%) | 42(51%) | 4(13%) | 4(12%) | 28(40%) | 17(40%) | 5(50%) | 28(39%) | 8(14%) | 14(23%) |
| Doctors | 13(24%) | 18(35%) | 30(52%) | 16(26%) | 16(32%) | 29(59%) | 20(26%) | 17(43%) | 24(56%) | 21(31%) | 15(35%) | 25 | 28(39%) | 8 (15%) | 25(42%) |
| Total | 51 | 52 | 58 | 62 | 50 | 49 | 80 | 39 | 42 | 69 | 43 | 49 | 63 | 53 | 60 |

**Vancomycin**

| **Profession** | **Aminoglycosides** | | | **Furosemide** | | | **Colistin** | | | **Theophylline** | | | **Tetracycline** | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know | Correct | Incorrect | Don't Know |
| Nurses | 27(23%) | 4(57%) | 19(50%) | 3(7%) | 27(35%) | 20(49%) | 18(31%) | 6(18%) | 26(38%) | 7(13%) | 6(32%) | 37(41%) | 6(13%) | 14(25%) | 30(52%) |
| Pharmacist | 47(41%) | 1(17%) | 2(5%) | 26(62%) | 20(26%) | 4(10%) | 23(40%) | 19(56%) | 8(12%) | 31(60%) | 5(26%) | 14(16%) | 31(65%) | 14(25%) | 5(9%) |
| Doctors | 42(36%) | 1(17%) | 18(45%) | 13(31%) | 31(40%) | 17(41%) | 35 (46%) | 9(26%) | 17(33%) | 14(27%) | 8(42%) | 39(43%) | 11(23%) | 27(49%) | 23(40%) |
| Total | 116 | 6 | 39 | 42 | 78 | 41 | 76 | 34 | 51 | 52 | 19 | 90 | 48 | 55 | 58 |

**Table-IV. Knowledge of Health Professionals Concerning Effects of Different Drugs on Vancomycin and Valproic Acid**

| Parameters | Value | Asymp. Sig. (2-sided) |
|---|---|---|
| **Anticoagulant (Warfarin)** | | |
| Aspirin | 12.732[a] | 0.013 |
| Antibiotic | 28.640[a] | 0 |
| Propranolol | 23.608[a] | 0 |
| Antacids | 22.542[a] | 0 |
| Vitamin E & C | 12.950[a] | 0.012 |
| Atenolol | 0.005 | 0 |
| Cholestyramin | 21.023[a] | 14.848[a] |
| Statins | 22.431[a] | 0 |
| **Valproic Acid** | | |
| Theophylline | 30.031[a] | 0 |
| Isoniazid | 36.319[a] | 0 |
| Aspirin | 14.666[a] | 0.005 |
| Carbapenems | 25.919[a] | 0 |
| Acetaminophen | 33.085[a] | 0 |
| **Vancomycin** | | |
| Furosemide | 32.538[a] | 0 |
| Colistin | 24.785[a] | 0 |
| Theophylline | 31.316[a] | 0 |
| Aminoglycosides | 22.317[a] | 0 |
| Tetracycline | 45.895[a] | 0 |

**Table-V. Statistical Summary of Professionals Responses Regarding Drug Interactions of Valproic Acid, Warfarin and Vancomycin**

## DISCUSSION

Both quantitative and qualitative modifications of one medicinal effect by other regarded as drug interaction.[21] Drug-drug interactions regarded as significant clinical dilemma. Increased prevalence of DIs reported annually with the preface of variety of new drugs. Many drug regimens and series of narrow therapeutic range medicines or drugs with low index of curative effect are further accountable to encompass rigorous drug interactions. Health-care professionals must be familiar and adequately perceptive to examine and tackle any severe outcome of the DIs in patients. A study suggested that nowadays, a variety of drugs are available commercially with widespread trend of poly prescriptions which may clearly integrate the probable drug interactions and resultant effects could be risky or cause treatment failure.[22]

| Drugs | | Sum Squares | df | Mean of Square | F | Sig. |
|---|---|---|---|---|---|---|
| Aspirin | Inter Groups | 2.286 | 2 | 1.143 | 3.460 | 0.034 |
| | Intra Groups | 52.210 | 158 | 0.330 | | |
| Statins | Inter Groups | 1.543 | 2 | 0.771 | 1.616 | 0.202 |
| | Intra Groups | 75.451 | 158 | 0.478 | | |
| Isoniazid | Inter Groups | 20.493 | 2 | 10.247 | 17.495 | 0.000 |
| | Intra Groups | 92.538 | 158 | 0.586 | | |
| Antacids | Inter Groups | 6.819 | 2 | 3.410 | 7.677 | 0.001 |
| | Intra Groups | 70.174 | 158 | 0.444 | | |
| Propranolol | Inter Groups | 14.167 | 2 | 7.083 | 12.113 | 0.000 |
| | Intra Groups | 92.392 | 158 | 0.585 | | |
| Colistin | Inter Groups | 10.340 | 2 | 5.170 | 7.047 | 0.001 |
| | Intra Groups | 115.909 | 158 | 0.734 | | |
| Cholestyramine | Inter Groups | 12.561 | 2 | 6.280 | 9.757 | 0.000 |
| | Intra Groups | 101.700 | 158 | 0.644 | | |
| Carbapenems | Inter Groups | 16.321 | 2 | 8.160 | 13.771 | 0.000 |
| | Intra Groups | 93.630 | 158 | 0.593 | | |
| Furosemide | Inter Groups | 15.716 | 2 | 7.858 | 18.454 | 0.000 |
| | Intra Groups | 67.278 | 158 | 0.426 | | |
| Vitamin E & C | Inter Groups | 7.095 | 2 | 3.548 | 6.034 | 0.003 |
| | Intra Groups | 92.892 | 158 | 0.588 | | |
| Atenolol | Inter Groups | 2.371 | 2 | 1.185 | 2.752 | 0.067 |
| | Intra Groups | 68.039 | 158 | 0.431 | | |
| Antibiotic | Inter Groups | 0.735 | 2 | 0.368 | 0.612 | 0.544 |
| | Intra Groups | 94.954 | 158 | 0.601 | | |

Table-VI. Analysisof variance (anova) of participants answeres for interactions of valproic acid, anticagulants and vancomycin with related moities

| Parameters | Physicians (N=61) | Nurses (N=50) | Pharmacist (N=50) |
|---|---|---|---|
| Score | Frequency | Frequency | Frequency |
| 1 | 35 | 15 | 32 |
| 2 | 18 | 25 | 12 |
| 3 | 6 | 6 | 3 |
| 4 | 2 | 2 | 2 |
| 5 | 0 | 2 | 1 |
| Mean Score | 1.590.16 | 2.020.83 | 1.549.02 |

Table-VII. Mean scores for perception of professionals regarding DDIs
Note: Score 1=agreed, 2=strongly agreed, 3=neutral, 4=disagreed, 5=strongly disagreed

Another investigation demonstrated the effects of narrow therapeutics agents and declared that their slight variation in systemic absorption may lead significant alteration in pharmacodynamics response.[24] According to a study, individuals who receive narrow therapeutic index drugs must be strictly advice to screen out the optimal treatment and potential drug-drug or drug-nutrient interactions.[11,23] Another study presented the necessity to focus the role of health related professionals mainly physicians, pharmacist and nurses who remain interlinked with patients.[11]

Hence, clinicians must have strong understanding about potential interactions. Generally during clinical practice, it is almost impracticable for health carers to retain full DIs information so the current study mainly emphasised to explore and come close to the consideration of allied health care experts pertaining to DIs. Recent study showed half number of female participants (46.8%) with average mean age of 31 years. In another study similar cohorts were selected to assess the awareness about the drug-diet interactions infatuated by doctors, nutritionists,

pharmacists and nurses regarding anticoagulant therapy.[10,11]

Drug interactions may develop the scope of challenge for clinicians in routine practice. The majority of pharmacies utilize the DIs software programs resources with their dispensing package. Many scientific researches proven the function of Drug Interaction Checker" Micromedex® online drug reference, Lexi-Interact in Lexicomp®, in Natural Medicines Comprehensive Database® (NMCD®) and software which are controlled by the pharmacists to monitor patients for DDIs.[25-27] The sources utilized by the study participants to assess DDIs during handling, inscription and interpretation of prescription are given in Table-II(a). The drugs were entered one by one into the software through patient's medical profiles to interpret the interacting drug combinations. About 64% nursing employee recall DIs based on their memory comparative to 13% doctors and 10% pharmacists. However, an additional source to acquire DIs based on relevant books for references along with memory comprised 39 % for physician and 30% for nurses. Pharmacists always engage in recreation of health care system and characterized as drug custodian by having sufficient medical knowledge and using computerized screening system. Pharmacists also have enormous medical background and their personal experiences are accountable when other services are not available.[28] There is no existence of single method to make possible the practicing professionals against the avoidance of DIs in routine clinical practice. In clinical practice, health care professionals must ensure the awareness of DIs to minimize probable side effects in patients.

Perception in terms of mean scores was calculated by likert scale approach and found 1.549.02, 1.590.16, and 2.020.83 for pharmacist, doctors and nurses correspondingly (Table-VII). Significant magnitude of interaction of anticoagulant (warfarin) has been reported with vitamins E and C, different groups of antibiotics, aspirin and antacids. Warfarin utilization becomes greater than before in recent few years.

Antibiotics are frequently given among warfarin users that may potentiate the effects of warfarin. Similarly co-administration of warfarin and aspirin may generate the risk of bleeding so usually such combination cannot be ignored.[26,29] The findings of a trial described the DIs among warfarin, vitamin C and E. The combination of such administration may decrease the anticoagulant consequence of warfarin along with various vitamins.[30] Assessment of DIs may vary among health professionals. The considerable right answer obtained with various respondent cohorts was variable and comparatively high with physician and pharmacist cohorts i.e., 56% and 47% and 53% and 38% in case of vitamin E and C and antacids with anticoagulants respectively. Figures-2 and 3 have shown inconsequential differentiation among physicians and pharmacist cadres in recognition of DIs, whereas most important differences were generated by cohort of nurses ($p < 0.05$).

In one study performed in 2000 in Massachusetts regions have shown the healthcare professionals awareness in interdisciplinary sections so that inadequate patient counselling or undesirable therapeutic consequences can be easily avoided.[3] The end result of study (2000) indicated that approximately 3.8% of emergency visits are actually due to DIs and remain a substantial cause of hospitalization.[31] The results revealed the association of clinical pharmacists in DIs assessments and having appropriate clinical facts at the end of study was effective to get better health outcomes of patients. A study decision acknowledged the advanced and improved knowledge of pharmacists for DDIs compared to nurses and doctors.[32] The various services offered by pharmacists involves dose adjustment, drug information, DIs screening and investigations which in turn direct and take part in managing anticoagulation therapy together for in/out patients in western countries.[33] Arithmetical portion of health experts responses concerning interaction of warfarin with cardiovascular and other drugs are summarized in Table-VI&VI.

Chi square χ² evaluation of participants and their

awareness for the effects of various drugs on valproic acid and vancomycin are mention in Table-V. On the other hand, a range of parameters like Pearson Chi-Square and likelihood ratio are calculated using p ☐ 0.05 for significant differences. Moreover, the combination therapy of isoniazid and carbapenems may alter the effects on serum concentration of valproic avid and recognized as one of important DIs. Isoniazid may increases and carbapenems decreases the serum concentration of valproic acid.[34-35] A further most frequent DIs reported with co- administration of vancomycin and theophylline involves severe dehydration, ache and kidney failure in acute phase of treatment while nausea, vomiting, GI discomfort and sepsis in long term.[36-37]

Comparative to other professions, clinical pharmacists endorsed their distinctive services for health care system expressed by correct DIs of vancomycin with colistin 40%, furosemide 62%, aminoglycosides 41%, tetracycline 65% and theophylline 60%. Only 7% nursing staff provided accurate reply for furosemide interaction with vancomycin. ANOVA test (Table 6) for participant's responses for related valproic acid, warfarin and vancomycin interactions was also carried out with dissimilar drugs to measure the group disparity of information. Study outcomes were observed considerably different among the study groups. P values throughout the study were kept ≤ 0.05.

The consequences of current study proposed the collaborative guidance and educational performance to enhance the perception and training of healthcare professionals in the vicinity of DDIs. Therefore, well defined and effective approach need to be initiated for the improvement and the implication of such critical issues in developing countries at different levels of wellbeing. Conversely, a referral predisposition in this study cannot be excluded. Hence, suggest larger cohort focused studies to support these findings.

## CONCLUSION

Identification of drug interactions (DIs) considered as leading challenge for health care providers, and it is practically not possible for everyone to memorize the entire potential interactions. Thus usual training sessions and incorporation of skilled knowledge associated to drug interactions among different healthcare personnel are essential to declare the suitable counselling of patient and optimal remedial outcomes. Pharmacists have a clear job responsibility in the detection and rectifying the DDIs and also advice, regulate or screening for the probable interaction-related adverse events. In the light of these facts further studies suggested to conclude the extent and degree/level of space with reverence to practices, knowledge and approaches amongst healthcare individuals in respective area. Such prospective investigations in future may be of significant worth to recommend preeminent strategies with basic rudiments in recognizing and managing possible interactions.

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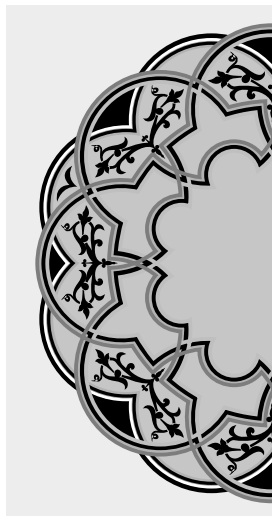
*"Attitude is a little thing that makes a big differences."*

**Winston Churchill**

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