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Original Research Article

Evaluation of knowledge, attitude and practice towards drug-drug interactions among postgraduates in tertiary care hospital, Kurnool

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ABSTRACT

Background: Drug-drug interactions (DDIs) are changes in a drug's effects due to concurrent use of another drug. Clinically significant interactions lead to undesired adverse effects, therapeutic failure, toxicity or may even cause death of the patients. The Aim is to evaluate the Knowledge, Attitude and Practice of Postgraduates regarding DDIs and implementation of educational program may enhance patient's safety.

Methods: A cross-sectional study was conducted among postgraduates in all clinical departments of Government general hospital, Kurnool in the month of October 2021. Pre-validated questionnaire was used to assess the KAP. It contains demographic data, knowledge and practice questions related to DDIs and attitude towards the preferable sources of drug interaction information. Data analysis was done by using SPSS version 26.

Results: Out of 220 questionnaires distributed, 126 postgraduates submitted with complete answers (n=126). Overall response rate is 57%. By using the Bloom's cut-off points, most of the respondents (43.5%) had low level of knowledge towards DDIs. Even respondents with high knowledge level (19%) are not practicing the drug interaction screening during the admission of patients. Majority of PGs with low level knowledge agreed to ask doctors than pharmacist about DDIs and prefer to search for DDIs using reference book than online mode as the source of drug information.

Conclusions: In my study, most of the respondents had insufficient knowledge to prevent life threatening DDI's. So, there is a need to increase medical educational program regarding the importance of screening and assessing of DDI's before prescribing medicines.

Keywords: Drug-drug interactions, Polypharmacy, Blooms cut off point

INTRODUCTION

Pharmacovigilance aims to improve patient's care and safety by identify and quantify the risks associated with the use of drugs, most importantly adverse drug reactions (ADRs).¹ Duration of hospitalizations may increase due to ADRs.² Drug-drug interactions (DDIs) are one of the commonest causes of ADRs, are common in the elderly people due to polypharmacy. Polypharmacy is the risk of clinically relevant drug interactions, which can induce the

development of ADRs, and both reduce or increase the clinical efficacy thereby it increases the complexity of therapeutic management.³ Drug-drug interaction (DDI) is defined as 'the pharmacological or clinical response to the administration of a drug combination different from the anticipated known effects of the two agents when given alone.'⁴ The combined drugs may be taken for the same disease or two different diseases present at the same time. The development of interaction depends on several conditions like Elderly age due to polypharmacy, Co-

morbidities like cardiovascular diseases or underlying disease condition of the patients like liver or kidney disease, the dose and duration of the medications. Clinically significant interactions lead to undesired adverse effects, therapeutic failure, toxicity or may even cause death of the patients.³

DDIs are classified into two groups

Pharmacokinetic DDIs: These interactions alter the concentration of the object drug at its site of action and consequently the intensity of response by affecting its absorption, distribution, metabolism or excretion. **Pharmacodynamic DDIs:** These interactions derive from modification of the action of one drug at the target site by another drug, independent of a change in its concentration. This may result in an enhanced response (synergism), an attenuated response (antagonism) or an abnormal response.⁵

There are many instances of rare but serious DDIs that could occur. Clinical effect of DDIs between clopidogrel and proton pump inhibitors was reported periodically.⁶ Concomitant use of isotretinoin and tetracycline cause rare but life-threatening intracranial hypertension due to additive mechanism was also reported.⁷ In addition, the use of sildenafil products sold as over the counter (OTC) drug in patients taking nitrates, may lead to a serious drop in the blood pressure by reducing pulmonary vascular resistance and by enhancing NO mediated vasodilatation.⁸ Increased risk of bleeding resulting from concomitant use of ketorolac and low molecular weight heparin.⁹ Macrolide antibiotics increases the effect of statins by inhibiting hepatic microsomal enzyme CYP3A4 metabolism leads to rhabdomyopathy.¹⁰ Chronic treatment with gemfibrozil and repaglinide may cause acute hypoglycemia.¹¹ Knowledge flexibility between PGs is due to different study backgrounds. Even in the same specialty, knowledge variation is due to years of experience and graduation place.¹² This study will investigate the possible factors related to the KAP of PGs towards the life-threatening drug-drug interactions.

Aim and objectives

Aim and objective of current study were to increase awareness of DDIs among clinicians to aid their role in screening and assessing the patients before prescribing medicines and to enhance the patient's safety.

METHODS

This was a Cross-sectional study was conducted over 1 month period October 2021 in Kurnool medical college, Kurnool. The survey forms were distributed and collected by Google forms over 2 weeks period to postgraduates of clinical department of GGH, Kurnool. A reminder was given to the non-respondents after the end of two weeks to increase the response rate. Pre-Validated questionnaire was used to assess the KAP. It contains demographic

data, knowledge and practice questions related to DDIs and attitude towards the preferable sources of drug-drug interaction information. The drug pairs that were asked in the questionnaire were widely used by the PGs in the wards and op. The sample size calculation was performed based on the nominal distribution. The data were analysed by using SPSS version 26. Descriptive analysis was used to compute frequencies of responses from all demographic items and questions on knowledge, attitude, and practice. The chi-square test was used for cross tabulation on the nominal level to explore the association between knowledge level and demographic data, attitude and practice, p value less than 0.05 was taken as statistically significant. The survey form was divided into four parts: Part 1 was the demographic characteristics of postgraduates, including gender and year of postgraduates. Part 2 was the evaluation of knowledge towards life-threatening DDIs, which are selected from Stockley's Drug Interactions Pocket Companion.¹³ The given score for a true choice was 1, for a false choice was 0, not sure choice was score 2. Assessment of Knowledge was done by Bloom's cut off points into high (80-100%), moderate (60-79%), low (<59%). Part 3 was evaluation of practice of PGs regarding DDIs. Assessment of Practice was done by 2-point Likert scale. Part 4 was evaluation of Attitude towards the preferred method for detection of DDIs. Assessment of Attitude was done by 5-point Likert scale.

RESULTS

Out of 220 questionnaires distributed, 126 postgraduates submitted the complete forms (n=126). So, the overall response rate is 57%. Majority of the respondents were female (67%) and doing 2nd year (71%) postgraduate degree in KMC. The response rate was described in (Figure 1).

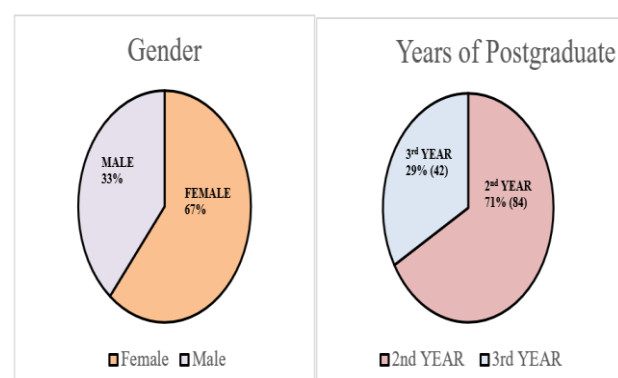


Figure 1: Response rate.

Assessment of knowledge among postgraduate towards DDIs

For the evaluation of knowledge, the respondents were asked about the predicted outcomes for ten drug pairs of drug-drug interactions.

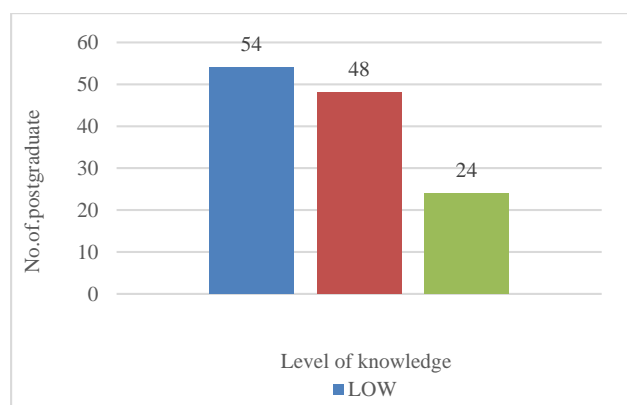


Figure 2: Score range for knowledge of postgraduate towards DDIs.

According to Bloom's cut off point, most of the respondents have Low level of knowledge towards DDIs. The highest correct answer was obtained for DDI of Warfarin and NSAIDs (78%), followed by DDI of sildenafil+isosorbide dinitrate (64%). The least correct answer was recorded for DDI between clopidogrel+omeprazole (21%), followed by DDI between azithromycin+simvastatin (31%). The highest incorrect answer was obtained for DDI of clopidogrel+omeprazole (45.2%) followed by DDI between ibuprofen+ ciprofloxacin (33%). The highest unsure answer was recorded for DDI of azithromycin+simvastatin (57%). The complete information of knowledge of PGs towards DDI was given

in the (Table 1). According to Bloom's cut off point, most of the respondents 43% (N=54) have Low level of knowledge towards Drug-Drug Interactions, 38% (N=48) had moderate level of knowledge and 19% (N=24) had high level of knowledge. Postgraduates with the score range of knowledge is summarized in (Figure 2).

Association between knowledge and attitude of PGs DDIs

Majority of PGs with low level knowledge agreed to ask doctors about DDIs and prefer to search for DDIs using reference book than online mode. Among high knowledge respondents, 50% agreed and 25% strongly agreed towards the use of online mode as the source of drug information. All groups strongly agreed and agreed to conduct frequent educational program about DDI. The attitude towards searching DDI information summarized in (Table 2).

Association between knowledge and practice of PGs towards DDIs

Regarding practice related to the detection and prevention of DDIs, 52% of the respondents were not practicing regular screening on DDIs during patients' admission. On the other hand, even PGs with high level knowledge were not doing assessment of drug interactions before prescribing or dispensing medications. Practice of PGs with the association with knowledge level related to DDIs were described in (Table 3).

Table 1: Knowledge of PGs towards drug-drug interactions.

Questions	Correct answers N (%)	Incorrect answers N (%)	Not sure answers N (%)
Clopidogrel+omeprazole=Increased risk of stroke	27 (21)	57 (45.2)	42 (33.3)
NSAIDs+warfarin=GI bleeding	99 (78)	6 (4.7)	21 (16.6)
Azithromycin+simvastatin=rhabdomyolysis	39 (31)	15 (12)	72 (57)
Ketorolac+heparin=Increased bleeding risk	66 (52.3)	15 (12)	45 (35.7)
Metoprolol+fluoxetine=shortness of breath	33 (26.1)	27 (21.4)	66 (52.3)
Ibuprofen+ciprofloxacin=Convulsions	27 (21.4)	42 (33.3)	57 (45.2)
Tetracycline+isotretinoin=Intracranial HTN	39 (31)	18 (14.2)	69 (54.8)
Digoxin+verapamil=Hallucination	42 (33.3)	24 (19)	60 (47.6)
Repaglinide+gemfibrozil=Severe Hypoglycaemia	42 (33.3)	18 (14.28)	66 (52.38)
Sildenafil+isosorbide dinitrate=Severe Hypotension	81 (64.28)	6 (4.76)	39 (31)

DISCUSSION

This study emphasizes only a few DDIs, involving relevant drugs in the clinical practice. In this study, there were associations between the level of knowledge among postgraduate study and years of experience. The

difference of level of knowledge among postgraduates are most probably due to the variability in the number of experience years. A study reported a lower DDI knowledge associated with a lack of clinical experience and this result supported the current study finding. Based on each question, the highest percentage of incorrect answers (45.2) was for clopidogrel and omeprazole DDI.

Table 2: Association between knowledge and attitude of PGs towards DDIs.

Attitude ^a	Knowledge level ^b			P value ^c
	Low	Moderate	High	
I prefer to search for DDIs using online mode				0.020*
Strongly disagree	6	3	0	
Disagree	9	12	3	
Neutral	15	3	3	
Agree	21	21	12	
Strongly agree	3	9	6	
I prefer to search for DDIs using reference book				0.001*
Strongly disagree	0	0	0	
Disagree	6	12	0	
Neutral	9	6	0	
Agree	36	18	12	
Strongly agree	3	12	12	
I prefer to ask doctors about DDI				0.001*
Strongly disagree	3	0	0	
Disagree	0	3	0	
Neutral	9	9	6	
Agree	39	18	12	
Strongly agree	3	18	6	
I prefer to ask the pharmacist about DDI				0.277
Strongly disagree	15	9	12	
Disagree	12	24	0	
Neutral	12	9	6	
Agree	15	0	3	
Strongly agree	0	6	3	
I prefer frequent educational program about DDI				0.007*
Strongly disagree	3	0	3	
Disagree	0	9	0	
Neutral	9	6	3	
Agree	21	18	9	
Strongly agree	21	15	12	

*Statistically significant, ^aAttitude questions based on 5 point Likert Scale, ^bBlooms cut-off point for knowledge (Low: <59%, Moderate: 60-79%, High (80-100%)). ^cp<0.05 using Chi-square test.

Omeprazole is frequently prescribed in the wards for ulcer prophylaxis. Clopidogrel is an antiplatelet agent used for CHD. Clopidogrel inhibits platelet aggregation by converting into active form by metabolising enzyme CYP2C19. When it is giving concurrently Omeprazole inhibits CYP2C19 so there is no conversion of active form of clopidogrel and decrease the effects of clopidogrel, it leads to increased risk of stroke. The highest percent of the Unsure answer (57%) was for the DDI of Simvastatin and Azithromycin. Rhabdomyolysis is a rare but potentially life-threatening adverse effect of statins. Consequently, the risk increases when statins are used concomitantly with Azithromycin that can increase their effects via interactions. So, it is essential to check the past medical history before prescribing medicines for current treatment. On the other hand, the lowest percent incorrect answer of DDIs was for NSAIDs and warfarin. NSAIDs are frequently prescribed in the wards and op as analgesics. Therefore, the PGs may be more aware and

familiar with its DDI. Regarding attitude, PGs preferred to ask Doctors about DDIs than Pharmacist. For searching, 50% of PGs using online mode and 50% of PGs using Reference books. In a study performed by Glassman et al almost 90% of clinicians believed that drug alerts would be useful to distinguish interactions.¹⁴ Generally, electronic medical record system, which provides alerts on interactions between drugs prescribed for the patients automatically, has proved an effective impact in another study.¹⁵

Apart from that, most PGs preferred frequent educational program in DDI monitoring. This will be useful especially for fresh graduates. Regarding practice, 52% respondents were not practicing the screening of patient's drug interactions at the time of admission. This leads to occurrence of toxic effects. It is important to assessing potential DDI before prescribing or dispensing, documenting DDIs and performing patient counselling related to DDIs.

Table 3: Association between knowledge and practice of PGs towards DDIs.

Practice	Yes/No ^a	Knowledge level ^b			P value ^c
		High	Low	Moderate	
Screening of patient's drug interactions during admission are performed regularly in my department.	Yes (60) 47.6	6 25	33 61	21 44	0.011*
	No (66) 52.4	18 75	21 39	27 56	
Assessment of drug interactions before prescribing or dispensing medications is a regular procedure in my department.	Yes (60)	9	30	21	0.288
	No (66)	15	24	27	
Documentation of reported drug interactions is a regular procedure in my department.	Yes (96)	18	42	36	0.963
	No (30)	6	12	12	
Patient counselling about the suspected drug interactions is a regular process in my department.	Yes (90)	18	39	33	0.902
	No (36)	6	15	15	

*Statistically significant, %The percentages are reported as percentages of knowledge, ^a2-point Likert scale, ^bblooms cut-off point for knowledge (Low: < 59%, Moderate: 60-79%, High (80100%)), ^cp<0.05 using Chi-square test.

However, there were many PGs who are neutrally related to these practices, especially among the PGs with a low level of knowledge. Steps necessity to be taken to make sure these practices are fully implemented by PGs to reduce DDIs. A study has suggested that adherence to correct policies or prescription writing, an appropriate surveillance system to monitor DDIs, and promoting physician's knowledge on potentially harmful DDIs should be practiced in preventing DDIs.

CONCLUSION

In this study, most of the respondents had insufficient knowledge to prevent DDIs. Frequent awareness programs regarding DDIs are necessary to enhance patient safety. Clinicians should be aware of patients' current drugs, including drugs prescribed by other clinicians and all OTC (over-the-counter) drugs before prescribing medicines. This ensures that any unforeseen interactions do not cause toxicity.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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