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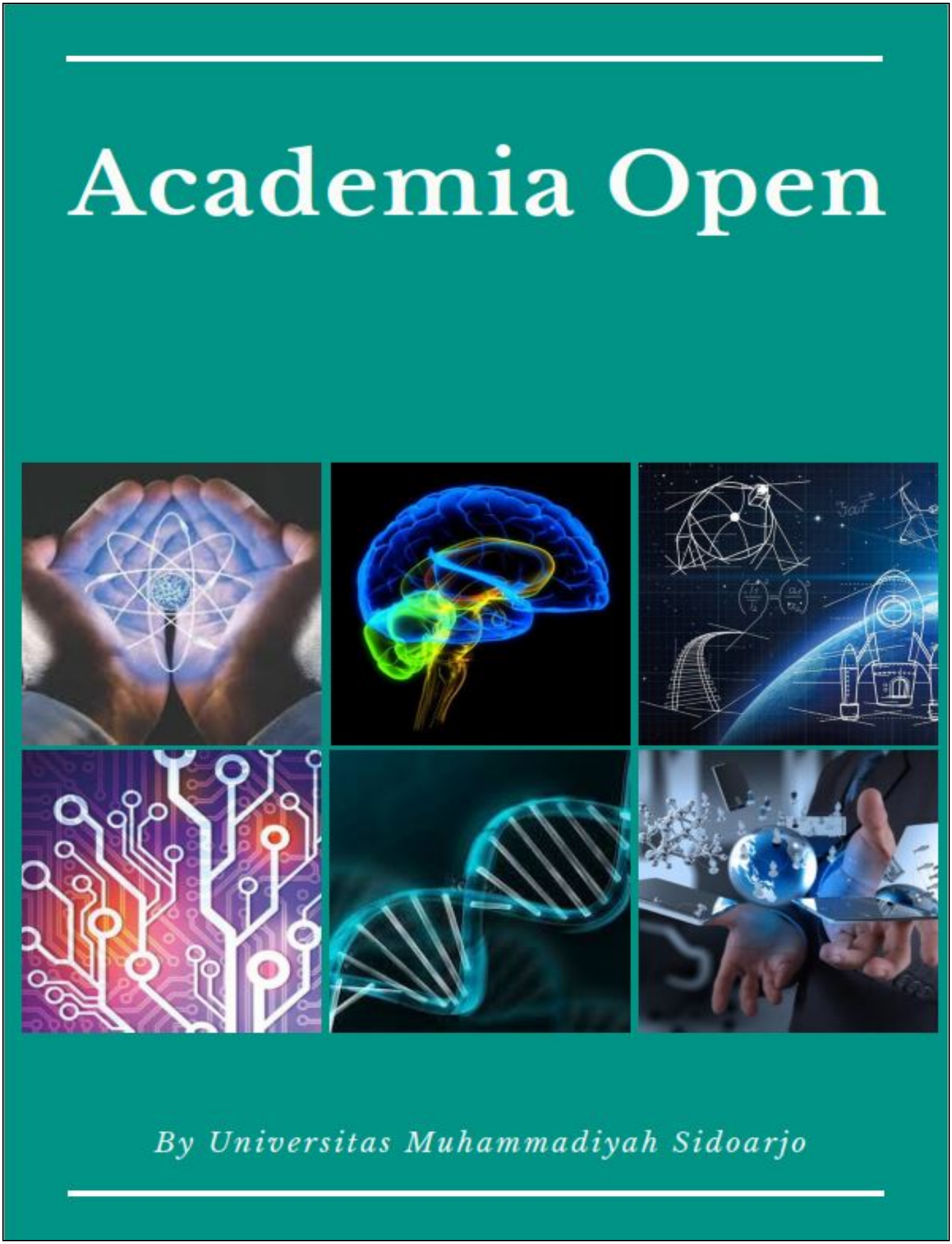

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Uncovering the Knowledge Landscape of Food-Drug Interactions Among Medical Professionals

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Abstract

Background: Drug-food interactions (DFIs) can alter drug pharmacokinetics and pharmacodynamics, impacting patient outcomes. Health care professionals (HCPs) play a critical role in managing these interactions. **Specific Background:** Despite their significance, the awareness of DFIs among Iraqi medical professionals is inadequately documented. **Knowledge Gap:** There is a lack of comprehensive studies evaluating the knowledge of DFIs among medical professionals in Iraq, which is crucial for improving patient care and therapeutic efficacy. **Aims:** This study aimed to evaluate the knowledge of food-drug interactions among Iraqi medical professionals, including medical students, newly graduated doctors, and junior doctors. **Methods:** A cross-sectional study was conducted using a self-administered questionnaire with 20 questions evaluating knowledge on common DFIs. **Results:** The study revealed a concerning lack of knowledge about DFIs among participants, with junior doctors scoring an average of 7.1 out of 15, newly graduated doctors 6.38, and sixth-grade medical students 5.27. Only 13% felt knowledgeable about DFIs, while 31.7% acknowledged their insufficient understanding. Notably, knowledge on interactions such as tyramine-rich foods with antidepressants and grapefruit juice with statins was limited. **Novelty:** This study provides the first comprehensive assessment of DFI knowledge among Iraqi medical professionals, highlighting significant gaps and educational needs. **Implications:** The findings underscore the necessity for enhanced educational programs targeting DFIs in medical curricula, ensuring HCPs are equipped to counsel patients effectively, thereby improving patient safety and therapeutic outcomes. These results emphasize the importance of targeted educational interventions to bridge the knowledge gap, ultimately contributing to better health outcomes and informed patient care in Iraq.

Highlights:

- Knowledge Gaps: Iraqi medical professionals lack understanding of common food-drug interactions.
- Education Needed: Enhanced training on interactions is essential in medical curricula.
- Patient Safety: Improving knowledge will lead to better patient outcomes.

Keywords: Food–Drug Interactions, Knowledge, Drug Interaction, Medical Students

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Introduction

The possible effects of food - drug interactions (FDIs) on patient well-being and therapeutic efficacy of the drug have drawn a greater spotlight in recent decades. Drug-food interactions might have adverse consequences on patient clinical outcome. Yet, there is no available information concerning the knowledge of food - drug interactions among health care professionals in Iraq.

The Food and Drug Administration (FDA) identifies food and drug interactions as interaction that can mainly change the pharmacokinetic and pharmacodynamic characteristics, and hence the therapeutic effects of certain medications [1].

And since there are many different pathways involved in the mechanism of how foods can affect the drug, they can be generically classified as either pharmacokinetic or pharmacodynamic interaction. Pharmacokinetic interactions refer to alterations in the drug's absorption, distribution, metabolism, or excretion, whereas pharmacodynamic interactions influence its effectiveness at the targeted site [2].

Through different manners, food can have an impact on drugs absorption. It may change the pH of the stomach, which may affect some medications' solubility and ionization. For instance, serum levels of ibuprofen, phenytoin, itraconazole, and methotrexate have been demonstrated to rise after consuming acidic beverage like cola; these interactions may be detrimental [3]

Food can also extend the time the medication takes to reach its site of absorption in the small intestine by delaying stomach emptying [4].

In addition, food particles have the ability to attach to medications in the gastrointestinal system, creating insoluble complexes that decrease drug absorption. Tetracycline antibiotics with dairy products, iron salts and antacid medications, have a well-known interaction in which these ions chelate the medication, reducing its bioavailability [5].

A further significant consideration in food-drug interactions is drug metabolism. Numerous medications undergo biotransformation, with the liver's cytochrome P450 (CYP) enzyme system being a key component. A change in CYP enzyme activity caused by a particular food can change how drugs are metabolized. The most prevalent CYP enzyme in the human liver, CYP3A4, is widely recognized to be inhibited by grapefruit juice. The primary mechanism via which statins and grapefruit juice interact is through cytochrome-3A4 (CYP3A4) inhibition. Interaction-related changes in plasma statins levels have the potential to potentiate statin adverse effects or lessen their therapeutic benefit. Consequently, it is usually advised that individuals taking statins not to consume grapefruit juice [6].

On the other hand, cruciferous vegetables like cauliflower, broccoli, Brussels sprout, cabbage, radish, and watercress can induce CYP enzymes, potentially reducing drug levels of some drugs like Propranolol, theophylline, zolpidem which are typical CYP1A2 substrates [7].

Food-drug interactions with pharmacodynamic properties can also have clinical implications. For example, tyramine-containing foods such as aged cheeses and cured meats might provoke hypertensive crises in people on monoamine oxidase inhibitor (MAOI) antidepressants such as Phenelzine, Isocarboxazid, Selegiline [8].

Another clinically relevant pharmacodynamic interaction occurs with vitamin K and warfarin, an anticoagulant medication. Vitamin K is required for the synthesis of clotting components in the liver, and consuming it can counteract warfarin's anticoagulant effects. To avoid changes in clotting times, patients using warfarin should maintain a constant intake of vitamin K-rich foods such as green leafy vegetables, Broccoli, Brussel sprouts and Avocado [9]. Fiber has been demonstrated in studies to bind to digoxin in the GI tract, limiting its absorption and bioavailability. This interaction is especially relevant with specific forms of fiber, such as wheat bran and psyllium [10].

Additionally, the timing of drug consumption with regard to meal influences its therapeutic effectiveness. For example, food can interfere with levothyroxine absorption in the digestive tract and extend the time it takes for levothyroxine to reach peak serum concentrations. So it is traditionally recommended to take the drug on an empty stomach for at least 30-60 minutes before mealtime [11].

Knowledge and awareness about these forms of interaction may be helpful in eliminating possible food-drug interactions. Junior doctors have an important role in educating patients regarding correct drug use, including information on food items to avoid while taking a specific drug. This role has the significance for maintaining patient’s safety and enhancing the impact of therapy. Several previous studied were conducted to evaluate health care professionals' understanding of common food-drug interactions, in different settings and countries. Alhubail et al. have examined the knowledge of healthcare providers and undergraduate students in Saudi Arabia's eastern region. The study showed that healthcare Professionals have a limited level of knowledge about specific diet and medicine interactions [12]. Another study among healthcare professionals working in Ethiopia's public hospitals

revealed that doctors, pharmacists , and nurse had insufficient knowledge and awareness of FDI. The mean knowledge score±SD of the provider was 28.6±6.6 out of an overall score of 59 [13].

One more survey included 200 randomly selected doctors separated into three groups (Professors, Post Graduates, and Interns) from Tertiary Care Hospital in India. The study provided that professors had greater levels of knowledge about FDIs than other. Intense training and knowledge incorporation among healthcare practitioners, particularly younger ones, is required [14].

a. Aim of the Study

The main objective of this research was to evaluate the medical professionals' knowledge of some of the most common food-drug interactions in Iraq.

b. Ethics Approval

Study participants verbally consented.

Method

A. Study Design

The most frequent food-drug interactions were the subject of this cross-sectional study, which was carried out using a confidential, verified self-administered questionnaire. A convenient sample of 230 doctor participated in the study. To confirm accurate sample representation, the physicians were chosen from various districts in Iraq. This inquiry was conducted between September 2023 and April 2024.

B. Tools used in the Research

The questionnaire, which be made of 20 questions, with some modifications, the questionnaire was created using a prior survey tool that was utilized in the published work by Radwan et al. [15]. The study involves some of the frequent and clinically significant interactions between food and the commonly used medications, which are prescribed by the physicians. Questions on the sociodemographic information, including age and gender were asked in the first part. The subsequent parts which include 15 questions were developed to determine the level of knowledge regarding drug-food interactions. The questions were closed-ended (yes/no/ not sure) about the concurrent administration of some medications with particular kinds of food and drinks. E.g. Do dairy products can reduce the absorption of certain antibiotics, like tetracycline? Is it safe to consume high amounts of vitamin K-rich foods, such as spinach, while taking warfarin? If consuming large amounts of garlic can increase the risk of bleeding when taking anticoagulant?

For every question correctly answered, one point was given; wrong response resulted in zero point. Each participant's knowledge score regarding food-drug interactions was determined by adding together all of the points. The sum of the results was used to determine the test's overall score. The knowledge questions have a maximum score of 15 overall.

C. Statistical Analysis

Using SPSS Version 28, the statistical analysis was conducted. Continuous variables were reported as mean±SD, while categorical data were presented as frequency. ANOVA, or one-way analysis of variance, was employed to compare the groups' total scores. A p-value of less than 0.05 was found to be significant.

Results and Discussion

A. Results

The questionnaires had been filled out by 230 health-care professionals. The ages of the participants were divided into three groups: (25.2% < 24 years, 71.7% were between 24-26 years, and 3 % of the participants were older than 26 years). Concerning sex, 59.5% of the participants were female and 40.4% were male. As regards to the scientific qualification of each group 74 were junior doctors who were working in different hospitals, 77 of them were newly graduated doctors and 79 were medical students in their last grade. About 55.2% of the participants were not sure if they have the adequate knowledge regarding food and drugs interactions, while 13 % thought that they have enough information. Furthermore, 31.7% of the participants felt that they don’t have sufficient knowledge in this topic. Most of them agreed that drug interaction with food has an important role in influencing the therapeutics outcomes (Table1).

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Characteristics		Frequency (n)	Percentage (%)
Age	< 24	58	25.2%
	24-26	165	71.7%
	> 26	7	3%
Sex	Female	137	59.5%
	Male	93	40.4%
HCPs	Six grade students	79	34.3%
	Newly graduated	77	33.4%
	Junior doctor	74	32.1%
Do you have enough knowledge about FDIs	yes	30	13%
	No	73	31.7%
	Not sure	127	55.2%
Do you think that FDIs can affect therapeutics outcome ?	yes	226	98.2%
	No	3	1.3%
	Not sure	1	0.4%

Table 1. ***Demographic Characteristics of the Study Sample***

By comparing the Knowledge of all groups. Approximately 58.1% of junior doctors correctly answered that Consuming excessive amounts of tyramine-rich foods, such as aged cheeses and cured meats, can raise the risk of hypertensive crises while taking certain antidepressants, such as phenelzine. Moreover, 83.7% of junior doctors agreed that patients consuming antibiotics such tetracycline should avoid milk, yoghurt and other dairy products. In addition, about 59.4% and 74.3% of the junior doctors recognized that patients on warfarin should avoid consuming high amounts of vitamin K-rich foods, such as spinach and kale and to avoid large amounts of garlic, respectively.

Regarding timing of food and drug consumption, only 37.9% of the medical students knew that levothyroxine should be taken on an empty stomach to ensure optimal absorption, On the contrary, the study showed a decline in knowledge of this identity as the degree progressed (32.4% for newly graduated doctors and 28.3% for junior doctors).

Once again, the group of students had more correct answers regarding the lack of effect of bananas and oranges on ACE inhibitors. Furthermore, 89.1% of the junior doctors correctly answered that the absorption of itraconazole is enhanced by a high-fat meal. As regards to the interactions between statins and grapefruit juice consumption, there was little knowledge of that Grapefruit juice could increase the level of statins. While more than half of participants understood the significance of abstaining from alcohol while taking metronidazole, junior doctors had the least amount of information.

All groups had shown little knowledge about the interactions between high-fiber diets and digoxin. In respect of the interactions of dairy products with some antibiotics such as tetracycline and ciprofloxacin, there was limited knowledge among the individuals involved. The respondents did not recognize precisely the interactions between grapefruit juice and other medications such as losartan and fexofenadine. The participants demonstrated a lack of knowledge about the influence of iron-rich meals on the absorption of specific antibiotics, like tetracycline, junior doctors showed a higher result about 40.5 %. As well as in concerning doxycycline administration the participants unaware of the connection between dairy products and doxycycline (Table 2).

Questions	Six th Grade Medical Students %	Newly Graduated Doctors %	Junior Doctors %	P Value
Tyramine-rich foods & antidepressants,phenelzine	50.6	40.2	58.1	
Dairy products & tetracyclines	48.1	62.3	83.7	
Vitamin K-rich foods & warfarin	40.5	53.2	59.4	
Garlic & anticoagulants	41.7	48	74.3	
Levothyroxine & timing of food intake	37.9	32.4	28.3	
Bananas,oranges&ACE inhibitors	22.7	12.9	20.2	

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High-fat meals & itraconazole	32.9	45.4	89.1	
Grapefruit juice & atorvastatin	16.4	24.6	22.9	
Alcohol & metronidazole	65.8	87	60.8	
High-fiber foods & digoxin.	16.4	32.4	33.7	
Dairy products & ciprofloxacin	37.9	40.2	40.5	
Grapefruit juice & losartan.	16.4	14.2	27	
Grapefruit juice & fexofenadine	12.6	31.1	13.5	
Iron-rich foods & tetracyclines	24	37.6	40.5	
Dairy products & doxycycline	31.6	36.3	27	

Table 2. ***Comparison of Knowledge About Food-Drugs Interactions among Health care professional groups***

Junior doctors scored 7.1 ± 2.75, newly graduated doctors scored 6.38 ± 3.53, and sixth grade medical students scored 5.27 ± 3 on the overall test (15 question). According to the one-way ANOVA test the results revealed a significant difference, p value < 0.005, (Table 3).

	Mean score percentage %	Mean ± SD	P value
six th grade medical students	32.9 %	5.27 ± 3	0.002
Newly graduated Doctors	39.8 %	6.38 ± 3.53	
Junior doctors	44.3 %	7.1 ± 2.75	

Table 3. ***The overall test score***

LSD post hoc test results revealed that there was significant difference between the junior doctors and the sixth grade medical students (p = 0.001), (Table 4).

	P value within the groups		P value
Six th grade medical students	Newly graduated Doctors	0.07	0.002
	Junior doctors	0.001	
Newly graduated Doctors	Junior doctors	0.33	

Table 4. ***Post Hoc tests***

The mean difference is significant at the 0.05 level.

Based on the study, it appears that none of the three participant groups knew much about the possible interactions between grapefruit and specific drugs, such as atorvastatin, losartan, and fexofenadine.

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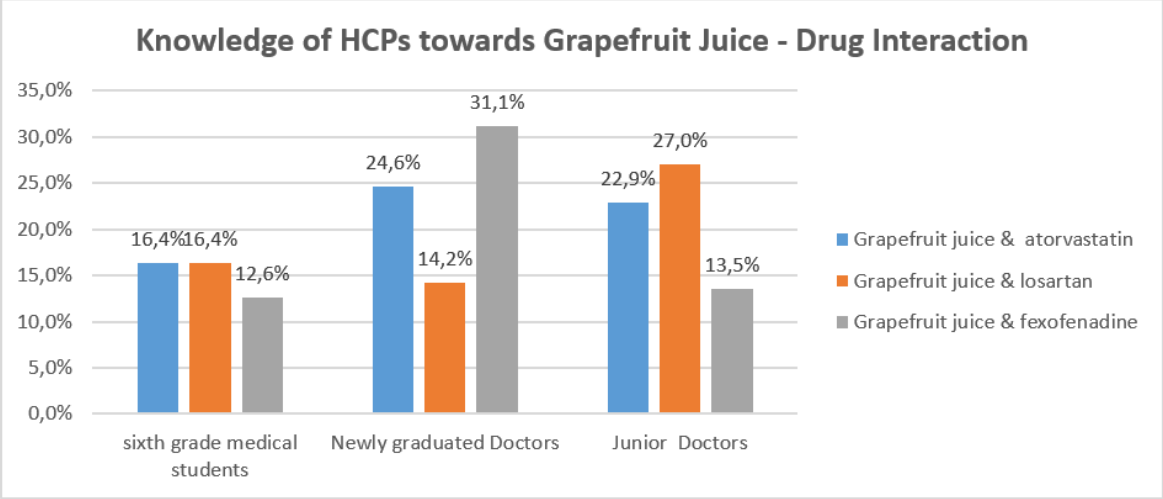

Figure 1. ***Grapefruit juice -drugs interactions***

B. Discussion

Assessing the healthcare professionals' knowledge of food-drug interactions was the goal of the current study conducted in Iraq. Since FDIs have a major impact on the safety and effectiveness of drugs, they are an essential component of patient care. Understanding the degree of knowledge possessed by medical professionals is crucial in detecting deficiencies and performing focused educational programs to enhance patient safety and treatment outcomes. According to the study findings, Iraqi medical practitioners' general knowledge regarding FDIs was inadequate.

The study involves three distinct groups from different stages of their medical careers: junior doctors working in different hospitals, newly graduated doctors, and medical students in their final year. Involving participants at various stages can provide an understanding to the improvement and progression of knowledge across time. More than half of the participants (55.2%) were unsure about their knowledge of FDIs. It is also notable that 31.7% of participants reported that they had little understanding in this field. Furthermore, just 13% of respondents stated they had enough knowledge about FDIs. This low percentage reinforces the need for more powerful education and awareness campaigns. The majority of professionals agree that eating particular foods while taking certain prescriptions can change the pharmacokinetic and pharmacodynamics properties of the drugs, affecting their efficacy and safety (Table 1).

In the current study, participants were asked to identify the most prevalent FDIs. The findings revealed that only 58.1% of junior doctors correctly identified that eating too many tyramine-rich foods, such as old cheeses and cured meats, can raise the risk of hypertensive crises when taking certain antidepressants, such as phenelzine. This gap in knowledge among the participant is noteworthy because it could result in poor patient education and potentially dangerous drug-food interactions.

While antibiotics are commonly prescribed, 83.7% of junior doctors provided that patients on antibiotics like tetracycline should avoid milk, yoghurt, and other dairy products. According to studies, having milk or other calcium-rich food within a few hours of taking tetracycline can limit antibiotic absorption [16].

Regarding food interaction with the anticoagulant warfarin. Patients on warfarin should maintain a consistent intake of green leafy vegetables to avoid fluctuations in their INR [17]. Only 59% of the junior doctors were aware to that interaction and the results were lower among the other groups. While there was a better knowledge concerning warfarin interaction with garlic, the anticipated mechanism behind this interaction is that garlic has antiplatelet aggregation effect [18].

Considering the timing of drug administration with respect to the time of meal ingestion. For maximum absorption, levothyroxine should be taken on an empty stomach, often 30-60 minutes before breakfast or 4 hours after the last meal [19]. According to the current results, just 37.9% of the medical students were aware of this serious time adjustment. Surprisingly, knowledge of this information decreased as the participants advanced in their medical professions, with just 32.4% of newly graduating doctors and 28.3% of junior doctors. This lack of understanding among medical workers may result in poor patient outcomes, emphasizing the need for increased education.

In addition, the participants demonstrated deficit knowledge by incorrectly answering that bananas and oranges do not have a significant effect on ACE inhibitors. Because of their potassium concentration, many people believe that eating bananas or oranges can interfere with the efficiency of ACE inhibitors. The American Heart Association

(2024) argues that a balanced regimen rich in fruits and vegetables is essential for preserving general health and treating hypertension. They do not advocate avoiding these fruits if you are using ACE inhibitors. [20]

Furthermore, several studies reported that the relative bioavailability and absorption of itraconazole increased when consumed with a fatty meal as opposed to fasting [21]. The fact that a large proportion of junior doctors accurately identified the link between high-fat meals and increased itraconazole absorption is encouraging. This information can enhance patient care.

Another important interaction is that grapefruit juice-statin- interactions which occur mostly via the inhibition of cytochrome-3A4 (CYP3A4), to some degree through suppression of P-glycoprotein [22]. The study revealed little knowledge among healthcare professionals about the interaction between statins and grapefruit juice. Previous research showed that only 21% of statin users often received information about statin-food interactions from their physicians [23]. Healthcare providers and patients should be informed about this interaction and take suitable precautions to decrease the likelihood of adverse effects.

However, over 50% of contributors can recognize alcohol-metronidazole interaction, even though junior doctors had the lowest knowledge about this topic, which draw attention to the necessity of improved training and education to assure patient safety. Likewise, there was evidence of ignorance of the interaction between digitalis and a high-fiber diet. Similar findings were reported by a previous study which revealed a lack of knowledge regarding drug food interactions [24]. Consuming digoxin alongside meals high in fiber content has the potential to reduce the body's absorption of digitalis by up to16- 32%, possibly resulting in inadequate therapeutic effects [25].

Additional important findings are the significant gaps in the knowledge about the interactions of commonly prescribed antibiotics with dairy product, such as tetracycline, doxycycline and ciprofloxacin. Tetracycline is a broad-spectrum antibiotic widely used to treat a variety of bacterial diseases. However, it has been demonstrated that tetracycline absorption can be greatly reduced when combined with milk and other dairy foods. This is because calcium and other divalent cations in dairy products create complexes with tetracycline, making it less accessible [26]. Doxycycline is an antibiotic belonging to the tetracycline class. Ciprofloxacin is a commonly used fluoroquinolone antibiotic. Ciprofloxacin, like tetracycline, can be decreased in absorption when taken with dairy products [27].

Minimal insights exist in relation to the interaction between grapefruit juice and certain blood pressure lowering medication such as losartan. The participants were unfamiliar with that interaction. losartan is an angiotensin II receptor blocker (ARB). By inhibiting CYP3A4, grapefruit juice can increase the bioavailability of losartan, leading to an increased risk of adverse effects, such as hypotension, dizziness, or hyperkalemia [28]. Patients using losartan should be cautioned not to consume grapefruit juice. This interaction should be known by medical professionals to ensure that the medication is taken both safely and effectively.

The existing study demonstrates little understanding regarding the effect of iron-rich meals on the absorption of specific antibiotics, like tetracycline. Tetracycline combines with iron as well as other divalent and trivalent cations to create stable complexes. In the digestive system, these compounds are poorly absorbed and insoluble. tetracycline’s' bioavailability is therefore greatly decreased when they are taken with iron supplements or meals high in iron [29]. Junior doctors displayed a higher level of knowledge (40.5%) than other participants, suggesting that medical education may play an important role. However, the overall lack of understanding among participants emphasizes the importance of increased education regarding this potential interaction.

The one-way ANOVA test results indicated a significant difference (p-value < 0.005) between the groups. This suggests that there is a real difference in the test performance of the three groups and that the variations in the mean scores are not likely to be the result of random variation. These findings are in line with earlier studies that demonstrated variations in medical professionals' competence and knowledge across various stages of their careers.

The mean scores of junior doctors and sixth-grade medical students differed significantly, according to the LSD post hoc test results ($p = 0.001$). According to this, junior doctors outscored medical students in the sixth grade on the 15-question exam. This finding is in line with the overall ANOVA results and can be attributed to the difference in clinical experiences and educational backgrounds.

The results of this research revealed that the three participant groups did not fully realize the possible interactions that grapefruit may have with some drugs, including atorvastatin, losartan, and fexofenadine (Figure 1).

This finding also accords with other earlier observations, which showed that community and hospital working pharmacists had unsatisfactory knowledge about common FDIs [30].

The participants' lack of knowledge underlines the need for more patient education and greater understanding of the potential risks of consuming grapefruit while taking particular medications. By giving patients more thorough information, medical professionals can assist people in making informed dietary choices and lessen the risk of adverse drug reactions or decreased medication efficacy as a result of grapefruit-drug interactions.

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Several reasons contribute to the lack of adequate knowledge, readily available medications and dietary supplements, insignificant coverage of FDIs in medical curriculum, and inadequate continuing education programs. Years of experience could also play a role.

And so on, the findings of this study have significant consequences for medical education and practice in Iraq by underling the importance of comprehensive FDI education within the educational medical curricula. It could be accomplished by the establishment of organized courses, case-based learning, focused training, and collaborative educational work and meetings to assess the newest findings in FDI treatment. By empowering future doctors with the required information and abilities, we may guarantee safer and more effective patient care.

Conclusion

Taken together, the current study indicates a lack of knowledge about FDIs among healthcare professionals. Additional studies should concentrate on establishing and assessing educational programs to address observed knowledge deficits as well as evaluate their effect on the health outcomes of patients.

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