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ORIGINAL ARTICLE

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Assessing Physicians' Knowledge Concerning Food-Drug Interactions in Sana'a City, Yemen

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ABSTRACT

Background: Certain foods and specific nutrients can interact with some drugs, potentially affecting their therapeutic efficacy and safety. A thorough understanding of food-drug interactions (FDIs) across various medical specialties is crucial in preventing these interactions in patients. Physicians have a key role in preventing these issues, as they are responsible for prescribing drugs and advising patients on dietary management. This study, therefore, aimed to investigate the knowledge of common FDIs and appropriate timing for drug administration among physicians in Sana'a City, Yemen.

Methods: A cross-sectional study was conducted from May to June 2021 among 499 physicians working in four public and two private hospitals in Sana'a City, Yemen. Data about physicians' FDIs and the timing of drug administration in relation to food intake were collected using a self-administered questionnaire. The Mann-Whitney U and Kruskal-Wallis H tests were used to determine the factors influencing physicians' knowledge of FDIs and appropriate timing of drug administration.

Results: Of the 499 physicians surveyed, 26.3% perceived that they had sufficient knowledge of FDIs. Most physicians correctly identified the interaction between caffeine and diazepam (79.6%) and the need to avoid potassium-rich foods with spironolactone (64.9%), followed by those who recognized interactions involving theophylline (59.3%) and tetracycline with milk (51.9%). Fewer physicians were aware of interactions such as grapefruit with amiodarone (30.3%) and atorvastatin (28.7%), wheat bran with digoxin (24.2%), and aged cheeses with monoamine oxidase inhibitors (27.7%). Most respondents correctly identified the appropriate timing for administering omeprazole (79.8%) and erythromycin (71.7%), followed by metformin (58.7%) and methotrexate (46.0%). Fewer answered correctly for propranolol (37.7%), levothyroxine (32.5%), calcium carbonate supplements (32.5%), isotretinoin (26.5%), glipizide (23.2%), griseofulvin (20.3%), and carbamazepine (12.8%). Physicians' knowledge of FDIs was significantly higher among physicians aged over 40 ($P = 0.046$) and consultants compared to their counterparts. Conversely, there were no statistically significant differences in physicians' knowledge of FDIs with respect to their gender, type of health facility, years of experience, or perceived knowledge of FDIs. On the other hand,

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physicians' knowledge of appropriate drug administration timing was significantly higher among older physicians, males, consultants, those working in private clinics, and those having 5–10 years of experience compared to their counterparts.

Conclusion: Physicians in Sana'a show insufficient knowledge of common FDIs, highlighting the need for targeted educational initiatives. Training should focus on interaction mechanisms, common examples, and prevention strategies, using case studies to promote practical application in clinical practice.

Keywords: Knowledge ▪ Food-drug interaction ▪ Drug administration ▪ Yemen

1. Introduction

Concomitant intake of certain foods or specific nutrients with drugs can influence drug pharmacokinetics, bioavailability, pharmacodynamics, and therapeutic efficacy.[1,2] The clinical significance of food-drug interactions (FDIs) is well-documented, with substantial evidence supporting their occurrence.[3] For instance, vitamin K-rich foods (e.g., leafy greens) antagonize warfarin's anticoagulant effect, potentially compromising clotting stability.[4] Similarly, potassium-sparing diuretics (e.g., spironolactone) or angiotensin-converting enzyme inhibitors, when combined with high-potassium diets (e.g., bananas, oranges), may precipitate hyperkalemia.[5] Dietary fiber can also impair absorption of drugs such as levothyroxine and digoxin.[6,7]

A study reported that 62.4% of patients experienced FDIs due to inappropriate drug timing relative to meals, with 13.3%, 18%, 7.7%, and 2% exposed to one, two, three, or four interactions, respectively.[2] Mechanisms underlying FDIs include inhibition of cytochrome P450 enzymes and phase II conjugation, altered gastric emptying, pH changes, drug-diet component complexation, and enzyme induction/inhibition.[8,9] Risk factors for FDIs among hospitalized patients include age, gender, education level, number of drugs, and disease duration.[10,11]

FDIs may reduce oral antibiotic absorption, leading to subtherapeutic concentrations and treatment failure. Grapefruit juice, for example, can increase adverse drug effects by more than fivefold.[12] Mitigating FDIs requires healthcare professionals (HCPs) to educate patients on label adherence, avoiding contraindicated foods/ beverages (e.g., alcohol, grapefruit juice), and proper dosing schedules.[13] Vigilance in prescribing for elderly or chronically ill patients, who face higher polypharmacy risks, is critical to minimizing FDIs.[14-17] Effective polypharmacy management involves evidence-based prescribing, interdisciplinary collaboration, and patient-centered care to optimize therapeutic outcomes.[18] Educational interventions improve HCP competence in FDI prevention. A study among pediatric nurses demonstrated significant post-training knowledge enhancement.[19] However, gaps persist, necessitating further education via drug interaction resources, software tools, and continuous training.[18-24] Limited pre- and post-graduate nutrition education among physicians and pharmacists contributes to insufficient FDI awareness.[25] While experienced clinicians exhibit better FDI knowledge, interns and postgraduates often lack proficiency.[24] Given physicians' pivotal role in preventing FDIs, assessing their awareness is essential. However, data on FDI knowledge among physicians in Sana'a remain scarce. Therefore, this study aimed to assess their awareness of FDIs.

2. Methods

2.1. Study design, population and setting

A cross-sectional study was conducted on the physicians from various specialties in Sana'a City. The study was conducted among physicians at hospitals in Sana'a. All physicians who willingly participated and completed the questionnaire were included. The study was conducted at four public and two private hospitals in Sana'a City, Yemen, from May to June 2021.

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2.2. Sample size and sampling strategy

Using the Raosoft® sample size calculator (www.raosoft.com), the minimum required sample size was estimated at 377 physicians, assuming a 50% response distribution, a 95% confidence level, and a 5% margin of error. However, 499 physicians were included in the study. Physicians from the six participating hospitals were selected via convenience sampling until the target sample size was reached.

2.3. Data collection

A pre-validated questionnaire, adapted from existing literature,[20,26] was slightly modified to fit the context of the current study. The updated tool underwent review by an expert panel, comprising a pharmacology educator, a registered dietitian, and a physician, to confirm its content validity. The panel evaluated the questionnaire for suitability, relevance, clarity, and its ability to effectively capture the necessary data. The finalized questionnaire consisted of four sections: socio-demographic and professional background of participants, general knowledge of physicians regarding food-drug interactions, specific knowledge of common food-drug interactions, assessed through close-ended questions ("Yes," "No," or "I don't know"), and understanding of proper drug timing in relation to food intake. Before distributing the questionnaire, physicians were briefed on the study's objectives.

2.4. Data analysis

The data were imported from an Excel sheet into IBM SPSS Statistics version 21.0 for Windows® (IBM Corp., Armonk, NY, USA). Categorical variables such as age, gender, physician professional degree, health sector, experience, working area, and income were presented as frequencies and percentages. The Mann-Whitney U test or Kruskal-Wallis H test, as appropriate, was used to assess the relationship between participants' demographic characteristics and their overall knowledge of FDIs, and appropriate timing of drug intake. A *P*-value of <0.05 was considered statistically significant.

3. Results

3.1. Characteristics of physicians

Less than half of the participants were under the age of 30 (46.7%), with a slightly higher proportion of males (53.9%). The majority were general practitioners (34.9%), followed by specialists (29.7%), residents (18%), and consultants (17.4%). Most respondents were employed in private hospitals (49.5%), while the remainder worked in public hospitals (33%) or private clinics (17.5%). Half of the participants had less than five years of professional experience (Table 1).

Table 1: Characteristics of physicians included in the study*

Characteristics	*n*	(%)
Age (years)		
<30	233	**(46.7)**
30–40	171	**(34.3)**
>40	95	**(19.0)**
Gender		
Male	269	**(53.9)**
Female	230	**(46.1)**
Professional degree		
Consultant	87	**(17.4)**
Specialist	148	**(29.7)**
Resident	90	**(18.0)**
General practitioner	174	**(34.9)**
Health facility type		
Public hospital	164	**(33.0)**
Private hospital	246	**(49.5)**
Private clinic	87	**(17.5)**
Years of experience		
<5	252	**(50.5)**
5–10	140	**(28.1)**
>10	107	**(21.4)**

*The total number of respondents was 499.

3.2. Perceived knowledge of FDIs

Of the 499 physicians participating in the study, 26.3% (95% CI: 22.4–30.4) perceived that they had enough knowledge about FDIs.

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3.3. Physicians' knowledge of FDIs

Most physicians were aware of the effects of caffeine on diazepam (79.6%) and the need to avoid potassium-rich foods with spironolactone (64.9%). Moderate awareness was noted for interactions involving theophylline (59.3%) and tetracycline with milk (51.9%). However, knowledge was limited for key interactions, including grapefruit with amiodarone (30.3%) and atorvastatin (28.7%), wheat bran with digoxin (24.2%), and aged cheeses with monoamine oxidase inhibitors (MAOIs) (27.7%) (Table 2).

3.4. Physicians' knowledge of appropriate timing of drug administration

Table 3 shows that most physicians correctly identified the appropriate timing for administering omeprazole (79.8%) and erythromycin (71.7%), followed by metformin (58.7%) and methotrexate (46%), propranolol (37.7%), levothyroxine (32.5%), and calcium carbonate supplements (32.5%). In contrast, a small proportion answered correctly for isotretinoin (26.5%), glipizide (23.2%), griseofulvin (20.3%), and carbamazepine (12.8%).

Table 2: Physicians' knowledge of FDIs in Sana'a City, Yemen (2021)*

FDIs	Correct answers n (%)
Amiodarone can be taken with grapefruit.	151 **(30.3)**
Atorvastatin can be taken with grapefruit.	143 **(28.7)**
Cauliflower consumption affects the efficacy of levothyroxine.	171 **(34.3)**
Caffeine consumption affects the efficacy of diazepam.	397 **(79.6)**
Patients can eat more leafy green vegetables with warfarin.	167 **(33.5)**
Patient taking theophylline should avoid excessive coffee and tea.	296 **(59.3)**
Milk affects the efficacy of tetracycline.	259 **(51.9)**
Patients taking MAOIs should avoid eating aged cheese.	138 **(27.7)**
Wheat bran diet affects the efficacy of digoxin.	121 **(24.2)**
Protein-rich foods affect the efficacy of levodopa.	151 **(30.3)**
Grapefruit juice can be safely consumed with all antibiotics.	226 **(45.3)**
Patients should avoid taking spironolactone with food rich in potassium.	324 **(64.9)**

*The total number of respondents was 499. FDIs, food-drug interactions. MAOIs, monoamine oxidase inhibitors.

Table 3: Physicians' knowledge of appropriate timing of drug administration in Sana'a City, Yemen (2021)*

Drug	Correct answers n (%)
Methotrexate	229 **(46.0)**
Carbamazepine	64 **(12.8)**
Isotretinoin	132 **(26.5)**
Omeprazole	398 **(79.8)**
Glipizide	116 **(23.2)**
Metformin	293 **(58.7)**
NSAIDs	148 **(29.7)**
Levothyroxine	162 **(32.5)**
Calcium carbonate supplement	162 **(32.5)**
Griseofulvin	101 **(20.3)**
Erythromycin	358 **(71.7)**
Propranolol	188 **(37.7)**

*The total number of respondents was 499. NSAIDs, nonsteroidal anti-inflammatory drugs.

3.5. Factors influencing physicians' knowledge of FDIs and timing of drug administration

Table 4 shows that physicians' knowledge of FDIs was significantly higher among physicians aged over 40 (P = 0.046) and consultants compared to their counterparts. Conversely, there were no statistically significant differences in physicians' knowledge of FDIs with respect to their gender, type of health facility, years of experience, or perceived knowledge of FDIs. On the other hand, physicians' knowledge of appropriate drug administration timing was significantly higher among older physicians (P <0.001), males (P <0.001), consultants (P <0.001), those working in private clinics (P = 0.001), and those who had 5–10 years of experience (P <0.001) compared to their counterparts.

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Table 4: Factors influencing the physicians' knowledge of FDIs and timing of drug administration in Sana'a City, Yemen (2021)*

	n (%)	Knowledge of FDIs			Knowledge of drug administration timing		
		Mean rank	Test value	*P*-value	Mean rank	Test value	*P*-Value
Age (years)							
<30	233(46.7)	248.37			219.23		
30-40	171(34.3)	238.44	6.145	0.046	271.25	21.4	<0.001
>40	95(19.0)	281.29			287.21		
Gender							
Male	269(53.9)	256.09	29297.5	0.302	276.49	23810.5	<0.001
Female	230(46.1)	242.88			219.02		
Professional degree							
Consultant	87(17.4)	313.46			293.64		
Specialist	148(29.7)	245.38	33.3	<0.001	281.63	35.8	<0.001
Resident	90(18.0)	273.04			249.04		
General practitioner	174(34.9)	210.28			201.78		
Health facility type							
Public hospital	164(33.0)	266.16			245.17		
Private hospital	246(49.5)	233.88	5.7	0.059	237.23	9.0	0.011
Private clinic	87(17.5)	259.41			289.51		
Years of experience							
<5	252(50.5)	241.64			221.57		
5–10	140(28.1)	253.59	2.1	0.343	301.38	28.6	<0.001
>10	107(21.4)	264.99			249.73		
Perceived knowledge of FDIs							
Yes	131(26.3)	263.29	22363.0	0.214	248.26	23876.0	0.870
No/unsure	368(73.7)	245.27			250.62		

*The total number of respondents was 499.

4. Discussion

To the best of our knowledge, this is the first study about the knowledge of physicians in Sana'a City about FDIs and the optimal timing for drug administration in relation to meals. Notably, there was a gap in physicians' self-assessed competency, as only 26.3% perceived their knowledge of FDIs as sufficient, with disparities in knowledge level according to professional degrees. These findings suggest insufficient training on FDIs during medical education or practice. The findings of this study are consistent with those of previous studies reporting inadequate knowledge regarding FDIs among doctors, nurses, and pharmacists.[20, 22, 25, 26, 28–30]

The knowledge of physicians was comparatively lower compared with that among pharmacists in Jordan (60%) and Palestine (61.7%).[26–29] However, the focus of the latter studies solely on pharmacists could potentially account for the disparity in knowledge levels. In Ethiopia and South Africa, the knowledge levels among HCPs were reported to be 48.4% and 49.3%, respectively.[22, 25] The findings of the present study revealed a lack of knowledge among physicians in recognizing specific FDIs and the timing of drug intake with regard to food consumption. For instance, only half of physicians knew the effect of milk on tetracycline, although it is well-established that the absorption of tetracyclines can be greatly reduced when consumed with dairy products such as milk and cheese.[31] This reduction is due to the chelation effect caused by cations like magnesium and calcium in milk.[32] Notably, when compared to findings from similar studies among pharmacists in Ethiopia (63.8%), Jordan (87.3%), and Palestine (94.2%),[22,26,29] it is evident that pharmacists

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demonstrated a relatively higher level of knowledge regarding this specific interaction and its underlying mechanism. Furthermore, less than a third (27.7%) of physicians in the present study recognized the need to avoid aged cheeses and fermented foods due to their interaction with MAOIs. This finding is consistent with studies conducted in Ethiopia and South Africa, where the majority of HCPs were unable to identify foods that interact with MAOIs.[22,25] One possible explanation for this lack of awareness could be the declining use of MAOIs as antidepressants in recent years. However, studies conducted exclusively in Jordan (68%)[26] and Palestine (71.8%)[29] revealed a comparatively higher level of knowledge concerning the interaction between MAOIs and aged cheeses or fermented foods.

Patients taking warfarin are advised to avoid green leafy vegetables that are rich in vitamin K, as these can interact with the drug's therapeutic efficacy.[31] In this study, about two-thirds of physicians mentioned that patients using warfarin could eat more green leafy vegetables, reflecting a gap in knowledge. Similarly, studies from South Africa and Ethiopia also reported that a substantial proportion of HCPs were unable to correctly identify foods that interact with warfarin.[22,25] Additionally, it is well-established that grapefruit can adversely affect the safety and efficacy of certain drugs, including amiodarone and atorvastatin.[33] Notably, less than one-third of the physicians in this study were aware of the interaction between grapefruit and these drugs.

Another important gap was observed in physicians' knowledge about the interaction mechanism between levodopa and protein-rich foods, highlighting the need to raise their awareness of the potential interactions between drugs and specific foods, as these can significantly influence patient safety and treatment outcomes. On the other hand, this study found that more than a third of the physicians correctly identified the appropriate timing for administering drugs in relation to food intake, highlighting a knowledge gap concerning proper drug administration practices. Similar findings have been reported from Ethiopia and South Africa.[22,25]

In this study, physicians aged over 40 and those holding consultant positions demonstrated significantly higher knowledge of FDIs compared to their younger and less experienced counterparts. This aligns with several previous studies, which suggest that age and professional seniority are positively associated with better awareness of clinical pharmacology principles, including FDIs. Older physicians and consultants likely benefit from greater cumulative clinical experience, repeated exposure to adverse drug events, and ongoing professional development, which may enhance their practical knowledge of FDIs. A study conducted in South Africa found that HCPs with longer clinical experience and higher qualifications were more likely to identify critical food-drug interaction scenarios correctly.[25] Similarly, senior HCPs were found to have higher FDI knowledge scores compared to junior staff, emphasizing the role of experiential learning.[22]

The lack of significant differences in FDI knowledge based on gender, type of health facility, years of experience, or self-perceived knowledge may indicate that knowledge gaps are widespread across demographic and practice contexts. This finding suggests that experiential exposure alone may not be sufficient unless accompanied by structured, targeted education and continuous medical training on FDIs. HCPs may still lack adequate training and reference resources to confidently identify and manage FDIs despite varying years of experience.[24]

This study also found that knowledge of appropriate drug administration timing in relation to food was significantly higher among older physicians, males, consultants, physicians working in private

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clinics, and those with 5–10 years of experience. These findings suggest that certain demographic and professional factors may influence the retention or prioritization of this specific knowledge domain. Notably, even the perception of having sufficient information did not show a statistically significant association with knowledge about FDIs or the appropriate timing of drug administration. For instance, food has been shown to reduce the bioavailability and peak concentration of isoniazid, potentially compromising the therapeutic efficacy of this anti-tuberculosis drug due to elevated gastric pH during food intake.[32,34] On the other hand, in this study, only about one-third of the physicians accurately identified that calcium carbonate and levothyroxine should be administered before meals, while less than one-third recognized that NSAIDs should be taken with food. Poor knowledge of drug administration time can lead to drug errors, jeopardizing both patient safety and treatment effectiveness.

This study provides baseline insights into the awareness of Yemeni physicians regarding FDIs and the appropriate timing of drug administration. However, it has several limitations that should be considered when interpreting the findings. First, data collection was primarily limited to Sana'a through convenience sampling, limiting the ability to generalize the results to other regions of the country. Third, reliance on self-reported data might introduce the possibility of social desirability bias, which may have influenced participants' responses. Additionally, although the questionnaire was adapted from previously validated tools, this study did not conduct a formal pilot test or calculate validity indices such as the content validity index or face validity index. Nevertheless, the questionnaire's validity is supported by its prior use in published research.

5. Conclusion

Physicians in Sana'a generally lack adequate knowledge of common FDIs, underscoring the need for improved education and awareness. Enhancing their understanding of these interactions supports more informed prescribing practices and effective patient counseling on dietary considerations. Training programs should cover essential topics such as the mechanisms of interactions, commonly encountered examples, and risk mitigation strategies, incorporating practical case studies to facilitate real-world application in clinical settings.

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Ethical approval and consent

Ethical approval for the study was obtained from the Research Ethics Committee of the Faculty of Medicine and Health Sciences at the University of Science and Technology, Sana'a, Yemen (MECA No: EAC/UST246). Prior to participation, physicians were given a clear explanation of the study's purpose, significance, and potential benefits. Participation was voluntary, and verbal consent was obtained following this explanation. Completion and return of the questionnaire were also considered an indication of informed consent. Participants were assured of their right to withdraw at any time and were informed that providing their names was not required. The questionnaire remained anonymous, and data were analyzed using coded identifiers only.

Conflict of Interest

The authors declare no conflict of interest associated with this article.

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