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RESEARCH ARTICLE

Psychiatrists' and Infectious Disease Physicians' Awareness and Knowledge Level of Drug-Drug Interactions Between Antiretrovirals and Psychotropics: A Comparative Questionnaire-Based Study

Nadir YALÇIN[*°], Ahmet Cağkan İNKAYA[**], Emre KARA[***], Koray BAŞAR[****], Özge KARADAĞ[*****], Kutay DEMIRKAN[******], Serhat ÜNAL[*******]

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SUMMARY

The incidence of drug-drug interactions (DDIs) increases with psychotropics in people living with HIV (PLWH). This study aimed to compare the knowledge of infectious disease physicians (IDPs) and psychiatrists about DDIs as a primary outcome and to assess their knowledge, attitudes and awareness of DDIs as a secondary outcome. The quantitative and comparative questionnaire methods were administered to IDPs and psychiatrists in Türkiye via online survey. The questionnaire included open-ended and multiple-choice questions on physicians' sociodemographic and attitudes to DDIs and three hypothetical case scenarios. Information including patients' age, sex, social and medical history, laboratory findings and all drugs were provided in each scenario. After providing brief DDI information, the case scenario question was asked again with pretest-posttest design. Attitudes of 31 IDPs and 29 psychiatrists on ART-psychotropic DDIs were examined. Thirty-five (58.3%) of physicians emphasized that their perceived competence in DDIs knowledge was 'average'. Moreover, 53 physicians (88.3%) were affected by DDIs on prescription behavior. When we asked physicians how often they informed their patients about DDI, 45 (75%) responded 'often/always'. Major DDI was correctly defined by psychiatrists [12 (41.4%) vs. 23 (79.3%)] and IDPs [24 (77.4%) vs. 29 (93.5%)] before and after providing brief DDI information ($p<0.001$). To the best of our knowledge, this is the first study comparing knowledge, attitudes and awareness of psychiatrists and IDPs towards antiretroviral-psychotropic DDIs. It was determined that the presence of DDIs influenced decision-making of physicians. The majority of physicians reported that they had an above average perceived (subjective) level of knowledge about DDIs, but their objective level of knowledge about a DDI was insufficient.

Key Words: *Antiretrovirals, Human Immunodeficiency Virus, People Living with Human Immunodeficiency Virus, Psychotropic Drugs, Drug-Drug Interactions, Knowledge Level*

Psikiyatristlerin ve Enfeksiyon Hastalıkları Hekimlerinin Antiretroviraller ve Psikotroplar Arasındaki İlaç-İlaç Etkileşimleri Konusundaki Farkındalık ve Bilgi Düzeyleri: Karşılaştırmalı Ankete Dayalı Bir Çalışma

ÖZ

HIV ile yaşayan kişilerde (PLWH) psikotroplarla ilaç-ilaç etkileşimlerinin (İİE) görülme sıklığı artmaktadır. Bu çalışmanın amacı, birincil sonuç olarak enfeksiyon hastalıkları uzmanları (EHU) ve psikiyatristlerin İİE'ler hakkındaki bilgilerini karşılaştırmak ve ikincil sonuç olarak İİE'ler hakkındaki bilgi, tutum ve farkındalıklarını değerlendirmektir. Kantitatif ve karşılaştırmalı anket yöntemleri ile EHU'lara ve psikiyatristlere online anket olarak Türkiye'de uygulanmıştır. Ankette hekimlerin sosyodemografik özellikleri ve İİE'lere yönelik tutumları ile ilgili açık uçlu ve çoktan seçmeli sorular ve üç varsayımsal vaka senaryosu yer almıştır. Her senaryoda hastaların yaşı, cinsiyeti, sosyal ve tıbbi geçmişi, laboratuvar bulguları ve tüm ilaçları içeren bilgiler verilmiştir. Kısa İİE bilgileri verildikten sonra, vaka senaryosu sorusu ön test-son test tasarımıyla tekrar sorulmuştur. 31 EHU ve 29 psikiyatristin antiretroviral-psikotropik İİE'lere karşı tutumları incelenmiştir. Hekimlerin 35'i (%58,3) İİE'leri konusunda 'ortalama' bir yeterlilik algısına sahip olduğunu vurgulamıştır. Ayrıca, 53 hekim (%88,3) reçete yazma davranışında İİE'lerden etkilenmiştir. Hekimlere hastalarını İİE konusunda ne sıklıkla bilgilendirdiklerini sorduğumuzda, 45 hekim (%75) 'sıklıkla/her zaman' yanıtını vermiştir. Majör İİE, bilgilendirme öncesi ve sonrasında psikiyatristler [12 (%41,4) vs. 23 (%79,3)] ve EHU'ları [24 (%77,4) vs. 29 (%93,5)] tarafından doğru tanımlanmıştır ($p<0,001$). Bu çalışma, psikiyatristlerin ve EHU'ların antiretroviral-psikotropik İİE'lere yönelik bilgi, tutum ve farkındalıklarının karşılaştırıldığı ilk çalışmadır. İİE'lerin varlığının hekimlerin karar verme süreçlerini etkilediği belirlenmiştir. Hekimlerin çoğunluğu algılanan bilgi düzeylerinin ortalamanın üzerinde olduğunu, ancak İİE'lerine ilişkin bilgi düzeylerinin yetersiz olduğunu belirtmiştir.

Anahtar Kelimeler: *Antiretroviraller, İnsan İmmün Yetmezlik Virüsü, İnsan İmmün Yetmezlik Virüsü ile Yaşayan Kişiler, Psikotrop İlaçlar, İlaç-İlaç Etkileşimleri, Bilgi Düzeyi*

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[*] ORCID:0000-0002-2280-8727, Hacettepe University Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara, Türkiye
[**] ORCID:0000-0001-7943-8715, Hacettepe University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Ankara, Türkiye
[***] ORCID:0000-0002-7034-4787,Hacettepe University Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara, Türkiye
[****] ORCID:0000-0003-4798-5305, Hacettepe University Faculty of Medicine, Department of Psychiatry, Ankara, Türkiye
[*****] ORCID:0000-0003-1372-1555, Bahçeşehir University, School of Medicine, İstanbul, Türkiye
[******] ORCID:0000-0002-6427-5826, Hacettepe University Faculty of Pharmacy, Department of Clinical Pharmacy, Ankara, Türkiye
[*******] ORCID:0000-0003-1184-4711, Hacettepe University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Ankara, Türkiye

[°] Corresponding Author; Nadir Yalçın,
E-mail: nadir.yalcin@hacettepe.edu.tr

INTRODUCTION

Mental disorders are 8 times more frequent among people living with HIV (Human Immunodeficiency Virus) (PLWH) than among the general population (Hill & Lee, 2013). Psychiatric disorders and psychotropic drug use could be as high as 50% and 27% among PLWH, respectively. Major depression can be found in up to 23% of PLWH, whereas its prevalence among the general population is 0.6% (Angelino & Treisman, 2001). Antidepressants are the leading co-medication used by 20.9% of PLWH, followed by anxiolytics (16.7%), antipsychotics (4.7%), and psychostimulants (3.0%) (Meade & Sikkema, 2005). Psychotropic drug usage is not related to the stage of HIV infection (Vitiello, Burnam, Bing, Beckman, & Shapiro, 2003). It is estimated that patient's adherent to psychotropic treatment is also adherent to antiretroviral treatment (ART) (Casaletto et al., 2016).

To minimize the risk of drug-drug interactions (DDIs) and to ensure safe and effective treatment, interventions such as dose adjustment, alteration of treatment or therapeutic drug monitoring should be performed or at least considered (Angelino & Treisman, 2001; Meade & Sikkema, 2005). The risk of potential DDIs is of concern as combination ART is recommended in the management of HIV infection which mandates physicians' awareness of the recognition and management of DDIs (Schlaeppi et al., 2020). The prevalence of red-flag DDIs among PLWH is 3.18% (Lopez-Centeno et al., 2019). While ART has gained notoriety for its association with a plethora of pharmacokinetic DDIs involving the CYP450 enzymes, the extent and clinical significance of these DDIs with psychotropics can vary, ranging from negligible effects on plasma concentrations to potentially life-threatening events like torsades de pointes, respiratory depression, or myelosuppression (Goodlet, Zmarlicka, & Peckham, 2019; Yalcin, Ak, & Demirkan, 2021). If psychiatric disorders and substance addiction cannot be managed accordingly, it may result in non-compliance.

It was recently shown that adherence to ART is high despite adverse effects which in turn, prone patients to drug-related adverse outcomes (Ceylan, Koc, Inkaya, & Unal, 2019). In line with the goals of the Joint United Nations Programme on HIV/AIDS (UNAIDS), no one should be left behind and any drug risks that impede outcomes should be eliminated. Commencement of a co-medication may lead to an increased risk of potential DDIs (Tseng & Foisy, 1999). It is estimated that 14.0% of PLWHs use more than 10 drugs simultaneously (Robertson, Penzak, & Pau, 2007), and polypharmacy is common among PLWHs (Hinkin, Castellon, Atkinson, & Goodkin, 2001; Kara, Inkaya, Aydin Hakli, Demirkan, & Unal, 2019; Mallet, Spinewine, & Huang, 2007). Polypharmacy enforces attending physicians' decision-making which results in overwhelmed physicians under the list of drugs and their potential DDIs. There are various online databases available for the determination of DDIs. Among them, *Liverpool HIV Interactions* (Liverpool Drug Interactions Group, Liverpool, UK) and *Medscape Drug Interaction Checker* (WebMD, New York, USA) databases were most commonly used. Different databases may reveal conflicting results which also incapacitate physicians' decision-making. In addition, understanding and implementation of DDI reports may also vary between clinicians, further affecting the management of PLWH.

It is essential that physicians are not only aware of DDIs, but also know the full details of DDIs and mitigation strategies and seek advice or prevention activities in these settings involving clinical pharmacists (Agu et al., 2014; Surmelioglu et al., 2021).

Limited data exist that address knowledge and attitudes of physicians about ART and/or psychotropic adverse effects and ART–psychotropic DDIs among PLWH. This study aimed to compare the knowledge of infectious disease physicians (IDPs) and psychiatrists about DDIs as a primary outcome and to assess their knowledge, attitudes and awareness of DDIs as a secondary outcome.

MATERIALS AND METHODS

A total of 60 physicians with at least 6 months of clinical experience in infectious diseases (IDs) or psychiatry were enrolled over 6 months period in Türkiye. These physicians were selected through the contact network of the ID physicians and psychiatrists involved in the study. The questionnaire was administered at different times to doctors in both groups who were blinded to each other. The questionnaire was administered electronically (Google® Forms) to both groups via e-mail groups. To determine the participants' baseline knowledge of the case scenario questions, the questionnaire was designed so that brief information would not be opened without a required baseline response. The questionnaire included open-ended and multiple-choice questions on physicians' sociodemographic (age, sex, academic degree, duration of experience in a medical specialty, institution, examination of PLWH with a mental health problem in the last 6 months) and attitudes to DDIs with a 5-point Likert scale (perceived competence in DDI knowledge, the effect of potential DDIs on prescription behavior and the frequency of informing patients about DDIs) and three different hypothetical case scenarios (Supplementary Material). The questions and case scenarios in the questionnaire were prepared by the research group, including clinical pharmacists, by utilizing current literature and drug information databases.

In these case scenarios, patients' age, sex, social and medical history, laboratory findings and all drugs were provided. In this direction, these case scenarios included three different types of DDIs (e.g., Case 1: major interaction requiring replacement or discontinuation of the drug, Case 2: moderate interaction requiring additional follow-up, and Case 3: minor interaction requiring no additional follow-up or intervention). Following the case presentations, physicians were asked whether there was any DDIs related to the case. If the physician thought of a potential DDI, then their attitudes and management strategies were questioned by multiple choice questions with hypothetical case scenarios. As it was estimated that most physicians use online sources to check DDIs, information on DDIs adapted from online sources (Liverpool HIV Interactions Database, Medscape Drug Interaction Checker Database) were provided after survey questions (Supplementary Material).

The survey was designed so that volunteers could not see the brief DDI information before responding to the initial question. After providing brief information during the survey, the case scenario question was asked again. Brief information on severity, clinical implication and management of each DDI obtained from the current and scientific database Lexicomp® was given for each hypothetical case scenario after the pretest and before the posttest. The questionnaire took study participants 15-20 minutes to complete. There was no incentive to participate, and reminder e-mails were sent a week later only once to physicians who did not complete the survey. Additionally, the analysis of the study only included surveys that were fully completed (Supplementary Material).

Statistical analysis

As there is no precedent study in the literature, the sample size could not be calculated. Instead, the power was calculated considering the data obtained by correct answer change after to be briefed of ID physicians and psychiatrists. With an effect size of 0.50, 95% power, 5% margin of error, the power of the 2-group study was found to be 95.07% (G*Power Version 3.0.10). Thirty-five physicians for each group were selected for comparison. While making the selection, physicians with at least 6 months of clinical experience were randomly selected by utilizing the working network and collaborations of psychiatrists and ID physicians who were the authors of the study.

In descriptive statistics, mean (SD) or median (minimum-maximum) values were given for numeric variables, and number (percentage) values were given for categorical variables. The normality of continuous variables was tested using the Shapiro–Wilk test. After

data extraction, continuous variables were defined as the mean (SD) and median (min-max), depending on the result of normality test. Mann-Whitney U tests were used to compare numerical data, and chi-squared and McNemar tests were used to compare categorical data. For all tests, $p<0.05$ was considered statistically significant. IBM SPSS Statistics 23.0 software was used to analyze and evaluate the data.

Those who volunteered to participate in the study responded to the questions and provided informed consent. The study was approved by the Hacettepe University Ethics Committee (decision no: GO 18/304-37).

RESULTS and DISCUSSION

Demographics

Despite the reminder, 4 (11.4%) ID physicians and 6 (17.1%) psychiatrists left the questionnaire unanswered. A total of 60 physicians were included; among them, 38 were female (63.3%), the mean (SD) age was 34.21 (5.10) years. Thirty-one (51.7%) were IDPs and 29 (48.3%) were psychiatrists (Table 1). The median duration of professional experience was 6 years for both IDPs (range: 1-30) and psychiatrists (range: 3-20) and the majority of physicians (78.3%) were employed in a tertiary hospital. There was no significant difference between the medical specialists and residents regarding demographic features. Also, 25 (41.7%) participants had treated a PLWH with mental health problems in the previous 6 months. IDPs (58.1%) encountered more PLWH with mental health problems than psychiatrists (24.1%) in the last 6 months. The duration of professional experience was similar across specialties.

Table 1. Sociodemographic characteristics of the study groups

	Psychiatrists (n=29)	IDPs (n=31)	Total (n=60)	*p*
Age, mean (SD)	34.21 (5.10)	36.97 (8.88)	35.63 (7.37)	0.149
Sex, n (%)				
Male	16 (55.2)	6 (19.4)	22 (36.7)	0.009
Female	13 (44.8)	25 (80.6)	38 (63.3)	
Academic degree, n (%)				
Medical specialist	23 (79.3)	12 (38.7)	35 (58.3)	0.003
Medical resident	6 (20.7)	19 (61.3)	25 (41.7)	
Duration of experience in a medical specialty, median (min-max) (years)	6 (3-20)	6 (1-30)	6 (1-30)	0.150
Institution, n (%)				
Tertiary hospital	19 (65.5)	28 (90.3)	47 (78.3)	0.042
Secondary hospital	10 (34.5)	3 (9.7)	13 (21.7)	
Examination of PLWH with a mental health problem in the last 6 months, n (%)				
Yes	7 (24.1)	18 (58.1)	25 (41.7)	0.016
No	22 (25.9)	13 (41.9)	35 (58.3)	

IDPs: infectious disease physicians, PLWH: people living with HIV

General DDI information

Ninety percent of participants used online resources to learn about DDIs, and potential DDIs 'always or often' (88.3%) affected their prescribing decisions. Six physicians (10.0%, one psychiatrist and 5 IDPs) experienced an adverse drug reaction related to ART and psychotropic drugs.

Only 5 (8.3%) of the participants consulted a medical pharmacologist for information on drug-drug interactions (DDIs), while none consulted a pharmacist in their clinical practice. The reason why none of the participants consulted pharmacists for information on DDIs may be due to the recent introduction of clinical pharmacy practice within multidisciplinary teams in Turkey. Three-quarters of physicians stated that they had limited knowledge of DDIs and 35 (58.3%) reported moderate competence regarding DDI management. Three-quarters of physicians preferred to change psychotropic drugs upon encountering a DDI. After identification of a potential DDI, 45 (75%) often/always informed patients about potential DDIs and a potential DDI often/always affected prescribing decisions in 53 (88.3%). Psychiatrists used printed materials to check for DDIs more frequently than IDPs (p=0.019) (Table 2). Preferred information resources for physicians to determine the DDIs in given case scenarios are shown in Table 2. No significant relationship was found between the level of self-perceived competence and the frequency of informing patients about DDIs (p=0.343).

Table 2. Resource of information and attitude to DDIs among physicians

	Psychiatrists (n=29)	IDPs (n=31)	Total (n=60)	*p*
Preferred information resources on DDIs				
Internet	28 (96.6)	26 (83.9)	54 (90.0)	0.113
Smart device applications	12 (41.4)	20 (64.5)	32 (53.3)	0.073
Printed materials	15 (51.7)	7 (22.6)	23 (38.3)	**0.019**
Senior physician	9 (31.0)	9 (29.0)	18 (30.0)	0.866
Drug leaflet	5 (17.2)	5 (16.1)	10 (16.7)	0.590
Medical pharmacologist	1 (3.4)	4 (12.9)	5 (8.3)	0.198
Pharmacist	-	-	-	-
Perceived competence in DDI knowledge				
Above average/Very high	9 (31.1)	6 (19.3)	15 (25.0)	
Average	17 (58.6)	18 (58.1)	35 (58.3)	0.339
Very low/Below average	3 (10.3)	7 (22.6)	10 (16.7)	
The effect of potential DDIs on prescription behavior				
Often/Always	24 (82.8)	29 (93.5)	53 (88.3)	0.185
Never/Seldom/Sometimes	5 (17.2)	2 (6.5)	7 (11.7)	
The frequency of informing patients about DDIs				
Often/Always	20 (69.0)	25 (80.6)	45 (75.0)	0.296
Never/Seldom/Sometimes	9 (31.0)	6 (19.4)	15 (25.0)	
Evaluation of ART and psychiatric drug interactions by physicians				
I check DDI in every examination	7 (24.1)	8 (25.8)	15 (25.0)	0.881
I just check DDI when a new psychiatric drug is initiated.	21 (72.4)	22 (71.0)	43 (71.7)	0.901
I check DDI when an ART is added.	14 (48.3)	15 (48.4)	29 (48.3)	0.993
I never check for a DDI.	-	-	-	

Physicians' attitude to DDIs				
Alternating all drugs	-	-	-	
Switching all ART	-	-	-	
Switching interacting ART	1 (3.4)	7 (22.6)	8 (13.3)	
Switching all psychiatric drugs	1 (3.4)	1 (3.2)	2 (3.3)	**
Switching interacting psychiatric drug	24 (82.8)	21 (67.7)	45 (75.0)	
No change in any drug	-	-	-	
Other	3 (10.3)	2 (6.5)	5 (8.3)	

* Percentages were taken over psychiatrists, infectious disease physicians and total physicians.

** *p-value* cannot be computed because the standard error of the difference is 0.

ART: antiretroviral treatment, DDI: drug-drug interaction, IDPs: infectious disease physicians

Responses to clinical scenarios

A total of 6 DDI questions in 3 case scenarios were directed to physicians before and after the brief information provided. The mean correct answer rate among psychiatrists and IDPs was 1.97 (1.11) and 2.19 (0.79), respectively (p=0.313). Before information, the number of correct answers given by psychiatrists and IDPs was 0.62 (0.67) and 0.97 (0.48), respectively, and after information was 1.34 (0.67) and 1.23 (0.56), respectively (p <0.001).

Minor DDI was correctly recognized by 12.9% of IDPs but none of the psychiatrists. After brief information, the correct answer rate was 20.7% and 16.1% in psychiatrists and IDPs, respectively. Responses to the moderate DDI was not different between specialties and were not related to the information provided. Major DDI was initially defined correctly by 41.4% of psychiatrists and 77.4% of IDPs, respectively. After providing information, the correct response among psychiatrists and IDPs was 79.3% and 93.5%, respectively. After providing information, correct responses to only minor and major DDIs significantly increased among all physicians (p=0.001 and p<0.001, respectively).

There was no statistically significant correlation between the perceived level of knowledge (subjective assessment) and the number of correct answers to the case scenarios (objective assessment). Self-perceived competence level did not affect the correct decision rate (p=0.624). After being informed, the correct attitude among physicians who reported that potential DDI '*often/always affect their decision*' increased from 85.7% to 93.3%.

According to the specialty of physicians, their correct attitude rates before and after being informed are shown in Table 3.

Table 3. Distribution of physicians responding correctly to case scenarios

Cases	Specialty	Before information	After information	*p***
Minor DDI	Psychiatrists (n=29)	-	6 (20.7%)	*
	IDs (n=31)	4 (12.9%)	5 (16.1%)	1.000
	Total (n=60)	4 (6.7%)	11 (18.4%)	0.039
	P***	0.113	0.903	
Moderate DDI	Psychiatrists (n=29)	6 (20.7%)	10 (34.5%)	0.289
	IDs (n=31)	2 (6.5%)	4 (12.9%)	0.687
	Total (n=60)	8 (13.4%)	14 (23.4%)	0.180
	P***	0.140	0.095	
Major DDI	Psychiatrists (n=29)	12 (41.4%)	23 (79.3%)	0.001
	IDs (n=31)	24 (77.4%)	29 (93.5%)	0.125
	Total (n=60)	36 (60.0%)	52 (86.7%)	<0.001
	P***	0.010	0.140	

*The test could not be performed because the number of participants who answered correctly before the information was zero (not significant). ** within specialty, *** between specialties

DDI: drug-drug interaction, IDPs: infectious disease physicians

Here we have shown that physicians treating PLWH with psychiatric disturbances are not aware of potential DDIs which might be encountered during follow-up. Furthermore, the attitude to potential DDIs might change from physician to physician which may further hinder patient care. There are differences about DDIs between the US Food and Drug Administration and the European Medicines Agency or country-specific information. Therefore, healthcare professionals often rely on other sources (websites, apps) for their daily management of DDIs (Back, 2019). Our results indicate that despite physicians utilizing the same online sources to check and learn potential DDIs; their attitude to potential DDI-related risks is divergent.

According to the sociodemographic characteristics of both groups, differences between sexes, academic degrees and institutions were considered as chance associations due to the nature of the study design. The fact that ID physicians examined significantly more PLWH than psychiatrists was an expected result due to their specialty.

The complexity of ART regimens, adverse effects and inadequate reimbursement as well as DDIs are also identified as barriers to providing improved care (Defty, Smith, Kennedy, Perry, & Fisher, 2010). Potential and risky DDIs associated with initiating concurrent psychotropic drugs in PLWH are quite common (Vitiello et al., 2003). There is undoubtedly a risk of potential DDIs with ARTs as most psychotropic drugs are metabolized by cytochrome P450 (CYP) 3A isozymes whose activity may be inhibited or induced by antiretroviral agents (Cattaneo et al., 2018; Gallego, Barreiro, & Lopez-Ibor, 2012). Furthermore, some psychotropic drugs may inhibit the activity of CYP enzymes and act as instigators of DDIs when simultaneously administered with ARTs, thus creating a complex scenario that may lead to inadequate psychotropic or ART doses and, consequently, sub-optimal clinical responses (Gallego et al., 2012).

In this study, we evaluated the attitudes of clinicians to potential DDIs subjectively and as well as objectively. Despite more than 80% of physicians reporting an average/high level of perceived competence in potential DDIs, the first correct response to clinical scenarios was 0.80 (0.60) (whereas the full score should be 3). Furthermore, the correct response to clinical scenarios were 1.28 (0.61) after brief information. Physicians' level of perceived competence and objective DDI knowledge was not

related. Therefore, there is a fundamental gap in physicians' knowledge and attitudes toward DDIs. According to a study, 46% of general practitioners cited ART-related DDIs as a barrier to prescribing for PLWH, highlighting physicians' concerns (Defty et al., 2010).

(Nabovati et al., 2017) reported that physicians utilized books (42.7%) and smart device applications (33.5%) to check for potential DDIs. However, the ART field is an ever-changing field and new drugs emerge in the market faster than the book publishing rate. In this study, the internet (90.0%) and smart device applications (53.3%) are preferred over hard-copy-published resources. They (Nabovati et al., 2017) also observed that physicians used smart device applications (24.9%) and consulted pharmacists (11.7%) when their patients were exposed to potential DDIs. Clinical pharmacy is in its infancy in our country, so many physicians do not have access to clinical pharmacy consultation. That is why almost all physicians use online resources to check for potential DDIs.

Online resources pose several challenges to their users. Firstly, some of the results are not evidence-based in the light of clinical practice. Secondly, they report on pairs of medicines rather than all treatment regimens, which makes it difficult to manage patients from a broad perspective. Finally, they report potential DDIs using different nomenclatures. For example, any DDI may be described as 'contraindicated' in one database, while the same DDI may be described as a 'serious' interaction in another database.

According to van Stiphout et al., when task analysis, including electronic prescribing training, was performed for physicians (intervention group), the frequency of missed DDIs was less than the control group. This result may improve this situation by making available real-life examples of missed DDIs (van Stiphout et al., 2018). It is estimated that the frequency of potential and clinically significant DDIs will decrease with the increasing use of technologies such as machine learning, electronic health records, and alert systems in healthcare (Obermeyer & Emanuel, 2016).

In addition, the interpretation of potential DDIs and their relevance to the clinical experience of people in this field is of concern. Benni et al. recently showed that professors are more vigilant about drug-food interactions than their junior colleagues, and almost a third of clinicians' face drug-food interactions in clinical practice (Benni, Jayanthi, Basavaraj, & Renuka, 2012; Zawiah et al., 2020). Our findings demonstrate that the level of DDI knowledge and correct DDI management was not related to the seniority of the physicians.

In another study the attitudes of patients about drug-drug interactions were evaluated (Arumugam, Murali, Biju, & Thankachan, 2015). Three-quarters of patients did not believe there was a risk of interaction with other drugs and 58.0% started allopathic and other drugs without consulting their physicians, and 64.0% of the patients stated that they did not communicate regularly with their physicians.

In a study (Immadisetti, Poka, Rajesh, & Varma, 2016), there were 267 DDIs in 107 (44.6%) of 240 PLWH receiving ART. Of these interactions, 14 (5.2%) were contraindicated and 253 (94.8%) were found to require additional follow-up. In a prospective questionnaire-based study, 129 (38.6%) patients had at least one clinically significant DDI, which was not recognized and/or mismanaged in 56 (43%) patients (Kuemmerle et al., 2021). In another study, the search identified 82 PLWH concomitantly receiving antiretroviral and psychotropic drug treatment, 55% of whom had plasma psychotropic drug concentrations that were below minimum adequate plasma levels. The same result was found in only 26% of the samples taken from people without HIV infection (Cattaneo et al., 2018). These results suggest that physicians should be cautious about potential DDIs in PLWH with comorbid diseases, and may change doses or drugs if necessary.

In a study assessing how concerns about adverse effects and DDIs affects medication adherence in

transgender women living with HIV on both hormone therapy (HT) and ART, only 49% of transgender women living with HIV discussed ART–HT DDI with their provider. This highlights the need to improve ART integration due to imperfect ART combinations and limited provider communication (Braun et al., 2017).

Physicians are aware of the adverse effects related to DDIs and the incidence of adverse effects decreases with the drug education given to physicians (Agu, Oparah, & Ochei, 2012; Tetteh et al., 2017). The majority of psychiatrists (72.4%) and IDPs (71.0%) stated that they would check for a DDI when prescribing a psychotropic drug. At the same time, when they found ART-psychotropic DDIs, the majority of psychiatrists (82.7%) and IDPs (67.7%) stated that they would change the interacting psychiatric drug. This result shows that the physicians do not consider changing ARV regime and the majority of infectious physicians are considering interfering with the psychotropic drug even though this decision falls beyond the scope of specialty. Our findings reveal that many physicians overreact to potential minor and moderate DDIs whereas follow-up will suffice. Switching to a second-line regimen because of a minor/moderate risk of DDI may in turn hinder HIV suppression and immune recovery.

Familiarity with the potential interactions and adverse effects associated with certain antiretrovirals and psychotropic medications will empower clinicians to make well-informed prescribing choices, thereby enhancing the health and well-being of this vulnerable patient group (Goodlet et al., 2019). Despite strong guidelines, many patients continue to use ARTs with a high risk of toxicity and clinically significant DDI due to patient reluctance to change therapeutics. Therefore, it is imperative that clinicians encountering PLWH have knowledge of all commercially available ART agents and relevant potential DDIs. To minimize the DDI rate, it is recommended to use resources such as DDI databases (Lexicomp, Medscape, Micromedex, Liverpool, etc.), case reports, clinical trials, DDI alert programs integrated into electronic health record systems, and the development of clinical pharmacist-led antiretroviral stewardship programs (Billedo, Berkowitz, & Cha, 2016; Johnston, Heavner, Liu, Casal, & Akgun, 2023).

In a survey including non-psychiatrist HIV specialist physicians, they failed to routinely evaluate neuropsychiatric comorbidities, follow guideline recommendations, and use questionnaires, highlighting opportunities for improved detection and management in PLWH (Perez-Valero, Blanch, & Martinez, 2022). On the other hand, it is estimated that the integration of education-oriented clinical pharmacy practices in countries with PLWH using psychotropics will enable the identification, prevention and management of clinically significant DDIs.

CONCLUSION

In our study, we have shown that after providing brief information regarding DDI risk, physicians' attitude to DDI management has been improved. However, physicians tended to overreact to minor and moderate DDI risks which necessitated a clinical pharmacist/pharmacologist consultation. Also, we have evaluated the knowledge and attitudes of attending physicians towards DDIs between antiretrovirals and psychoactive drugs via three didactic case scenarios. We have performed this survey on 2-different specialist groups experienced in the care of PLWH. Our results stress the importance of external consultation in managing DDIs between antiretrovirals and psychoactive drugs.

Study Limitations

However, our results have some limitations, including their cross-sectional design and the limited number of participants. Nevertheless, this study will contribute to the literature and increase the awareness and perspective of psychiatry and infectious physicians, especially against DDIs. On the other hand, as there is no precedent in the literature, the sample size could not be calculated.

In this study, it was found that all of the physicians controlled potential DDIs, the presence of a DDI influenced their decision-making, had partial information about DDIs, and informed their patients about DDIs. Although the vast majority of physicians reported an above-average perceived level of knowledge, their attitudes towards a potential DDI were inadequate, necessitating consultation with a clinical pharmacist. This result indicates that information on the internet is highly questionable and that consulting with current evidence-based databases or clinical pharmacists rather than the internet will allow for more health responses for potential DDIs. It is estimated that repeated DDI training to be applied to psychiatrists and IDPs in clinical practice will improve the awareness and knowledge level of physicians against DDIs in PLWH.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS STATEMENT

ACI, NY, EK, KD contributed to design; ACI, OK, KB, SU contributed to conception; ACI, NY, EK, OK contributed to acquisition, analysis, or interpretation; KD, KB, SU contributed to interpretation; ACI, NY, EK drafted manuscript; KB, OK, KD, SU critically revised manuscript.

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