European Review for Medical and Pharmacological Sciences 2023; 27: 3230-3242

Caffeine addiction and determinants of caffeine consumption among health care providers: a descriptive national study

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Abstract. – OBJECTIVE: Caffeine is the most commonly used psychostimulant compound with a long history of worldwide consumption. Consuming low to moderate doses of caffeine is generally safe and quite beneficial; however, several clinical studies show that high doses could be toxic. Additionally, caffeine users can become dependent on the drug and find themselves unable to reduce consumption despite impending and recurrent health problems associated with continued use. This study was conducted to explore the prevalence, determinants, and positive and negative effects of caffeine consumption among governmental health care providers (HCPs) who were caffeine users. It aims to determine the frequency of caffeine dependence and addiction in the Kingdom of Saudi Arabia (KSA) in January 2020.

SUBJECTS AND METHODS: This cross-sectional study recruited 600 randomly selected HCPs from all regions of KSA, who fulfilled the selection criteria through a self-administrated, online-validated questionnaire composed of three main parts using the DSM-IV to diagnose dependence and probable addiction.

RESULTS: The majority of the studied HCPs were females (67.8%), nonsmokers (82.0%), and Saudis (80.5%), with a mean age of 35 years. According to the DSM-IV, the prevalence of caffeine consumption was 94.3%. Caffeine dependence was reported in 270 (47.7%), while 345 (60.9%) were diagnosed as addicts. The most commonly consumed caffeine-containing substances were coffee and its variants/types (70%), tea (59%), and chocolate (52%), with each person spending about 220 SR per week on them. The main reported adverse effects, in descending order, were sleep disturbances, stomach problems, and cardiac symptoms. The most positive effects reported of caffeine consumption were feeling active, alert, confident, and happy. These findings were significantly affected by sex, occupation, and general health.

CONCLUSIONS: Caffeine use, dependence, and addiction are common among government HCPs in KSA. Caffeine has both positive and negative effects on this population and further research is necessary to better understand the long-term consequences of caffeine consumption.

Key Words:
Addiction, Caffeine, Caffeine-containing drinks, Dependence, Healthcare providers, Kingdom of Saudi Arabia.

Abbreviations

Caffeinated drinks (CDs); Caffeine-Related Disorder Not Otherwise Specified (NOS); Generally recognized as safe, (GRAS); Health care providers (HCPs); Kingdom of Saudi Arabia (KSA); Not Otherwise Specified (NOS); Saudi Riyal (SR); Substance use disorder (SUD); The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5); The International Classification of Diseases (ICD-10); The ryanodine receptors (RyRs).

Introduction

Caffeine (1,3,7-trimethylxanthine) is a psychoactive agent, pharmacologically mild stimulant,

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and a natural substance extracted from the leaves and fruits of certain plants, e.g., Camellia sinensis, Khat, Cola Tree, Cassina Tree, Guayusa, Mate Bush, Yaupon, Guarana, Cacao Tree, and Damiana. Caffeine is found in most beverages, such as coffee, tea, soft drinks, energy drinks, and products containing varying levels of cocoa or chocolate. It is the most commonly consumed substance by many people all over the world. In the United States, about 80 to 90% of adults and children consume it regularly, while in Saudi Arabia (SA), it was about 70 to 88%[1-6].

Safe daily caffeine consumption is recommended for adults to be limited to less than 180 milligrams (mg) to maintain alertness and avoid increasing health risks[7]. Pregnant women should consume less than 200 mg per day because too much caffeine can lead to low birth weight in children or miscarriage. Children (12 years old and younger) should consume no more than 45 mg per day, while adolescents shouldn't consume more than 100 mg daily[8].

Average doses of caffeine (85-250 mg) produce psychomotor activating, reinforcing, and arousing effects that depend on their ability to antagonize the brake that endogenous adenosine imposes on the ascending dopamine and arousal systems[3]. Its usual dietary doses produce a range of positive subjective effects, including increased well-being, happiness, energy, and sociability, especially after the first dose that reverses withdrawal effects in daily caffeine users who abstain from consumption overnight[9,10].

Caffeine overdose occurs when it exceeds 400 mg in healthy people and varies depending on the age group[7]. Caffeine toxicity, whether intentional or unintentional, is relatively common around the world. Physicians and other medical personnel must be aware of caffeine toxicity in order to recognize and treat this condition appropriately. Caffeine intoxication, as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), presents with muscle twitching, anxiety, sleeplessness, increased urination, gastrointestinal trouble, excitation, psychomotor agitation, and tremors. In high doses, caffeine can cause hyperadrenergic syndrome, resulting in seizures and cardiovascular instability[11].

Caffeine consumers can become psychologically or physically dependent on it, which gives rise to harmful effects[4,5]. Caffeine addiction is a psychological or physiological dependence on the drug, which is identified by the impact of caffeine on a person's day-to-day functioning rather than by the actual amount of caffeine consumed each day. Caffeine is physiologically addictive when caffeine intake surpasses 250 mg for a prolonged period or when it is heavily used and upon abrupt cessation, patients experience withdrawal symptoms that manifest as flu-like somatic symptoms, headaches, difficulty concentrating, weariness, and dysphoria[3,12-15]. Rapid heartbeat, reduced motor function, and frequent or uncontrollable urination are all indications[4,5,16]. However, the DSM-V does not list caffeine addiction as a substance use disorder (SUD), but it does list it as a disease that needs more research. In addition, DSM-V defines caffeine withdrawal and encourages research for its diagnosis.

If at least, the first three of the following criteria are met within 12 months, there is a problematic or addictive pattern of caffeine consumption that causes clinically significant impairment or distress according to the DSM-V[17]: (1) A persistent desire to reduce or limit caffeine consumption, or unsuccessful attempts to do so; (2) Consistent caffeine consumption despite being aware of a health or psychological issue that may have been triggered or exacerbated by caffeine; (3) Withdrawal manifestations, as evidenced by one or both of the following: the typical caffeine withdrawal syndrome, using caffeine (or a chemically related drug) to alleviate or prevent withdrawal symptoms; (4) Caffeine is frequently consumed in higher doses or for longer periods than intended; (5) Repeated tardiness or absences from work or school due to caffeine use or withdrawal; (6) Consistent caffeine use in the face of ongoing or recurring social or interpersonal issues caused or exacerbated by caffeine's effects (e.g., arguments with spouse about the consequences of use, medical problems, cost); (7) Tolerance as outlined by one of the two following criteria; a significant increase in caffeine dosage is required to have the desired effect or significantly reduced effect after repeated administration of the same caffeine dose; (8) A significant amount of time is spent on tasks required to obtain, consume, or recuperate from the effects of caffeine; (9) Caffeine cravings or a strong desire to use it.

The diagnosis of caffeine dependence syndrome is recognized by the International Classification of Diseases (ICD-10). This condition is a group of behavioral, cognitive, and physical changes that occur after long-term drug use. These changes include a strong desire to use the

drug, problems with self-control, continued use despite negative effects, choosing drug use over other activities and responsibilities, increased tolerance, and sometimes a physical withdrawal state[18].

There are no obvious hazards related to caffeine addiction in otherwise healthy adults. Nevertheless, there are extra health risks connected to caffeine-containing beverages because of the significant amount of white sugar found in colas and energy drinks[15,19]. Caffeine addiction frequently only lasts a short while, is more closely linked to overdose than to true caffeine dependence, and can be treated at the most basic level with knowledge. That's why learning about the effects of caffeine and adopting a healthy lifestyle that reduces caffeine consumption and promotes healthy sleep patterns are all potential treatment strategies[20].

Over the past ten years, caffeine-containing products have become more and more popular, and caffeine users started suffering from clinically significant disorders, such as caffeine dependency (more than 30%) and/or addiction[18,21-23] which have led to growing worries about the effects of long-term consumption on public health. Furthermore, it is unclear how or why some individuals are more or less prone to substance abuse and addiction, where escalation and reinitiation are two fundamental behavioral patterns that characterize abuse and result in addiction[24]. More investigation is required to ascertain the reliability, validity, and prevalence of this clinically significant health issue, particularly in special populations working in stressful environments.

Saudi Arabia's population consumes an average of 0.9 kilograms of coffee and tea per person each year representing the 10th-highest figure among Arabic countries. Previous studies[4,5] have reported high levels of caffeine consumption among healthcare workers. Health care professionals (HCPs) in SA became worried about caffeinated drinks (CDs) because of the bad effects of too much caffeine use. Therefore, we conducted this online survey in January 2020 among governmental HCPs from the 20 health regions in the SA to determine the frequency of caffeine consumption, to study the context of caffeine consumption, including sources and quantities, to explore caffeine's positive and negative effects among HCPs who are caffeine users, and to determine the frequency of caffeine dependence and addiction.

Subjects and Methods

Study Design and Participants

To achieve the study's objectives, a cross-sectional study in January 2020 targeted all governmental healthcare providers of both sexes, different specialties (nurses, pharmacists, public health technicians, applied science specialists, and physicians), and different age groups (18 years un to 60 years) from all over the SA (56080) during January 2020. Refusal to participate in the study, internet non-users, HCPs under the age of 18, retired HCPs, non-governmental HCPs, and those on vacation during data collection were all excluded.

The Sample Size

The sample size was computed using the Open Epi website, with a total target of 56,080 governmental HCPs from all over SA according to the General Authority of Saudi Statistics (2016)[26], with a precision of 0.5% at a 95% confidence level and an 80% power of the study. The prevalence of energy drink consumption was found to be 70%[19] among adults in northwestern Saudi Arabia. Then, to represent the 20 health regions in SA and different HCPs, it was duplicated to 600 HCPs to increase the study's impact.

Sampling Method and Data Collection Method

Using the multistage sampling method, the data were collected through an online, self-administered questionnaire *via* Google Forms, which was used in its creation, distribution, and collection. The URL is: https://docs.google.com/forms/u/0/d/e/1FAIpQLSf9MJOeHy_zaanTMzUND7pjlBx8JPOaA9kMuzBhP1IWgv0CA/closed; the form was shared *via* the HCP s' professional groups and the official platforms of many health care settings on WhatsApp, Twitter, and official emails. To increase the response rate, we randomly selected 10 HCPs from randomly selected governmental healthcare facilities in each of SA's 20 health regions. Reminder messages and follow-ups were sent every Friday for two months until the sample size was achieved.

Data Collection Tool

The survey was developed in English based on previous studies[17-20], then translated into Arabic by a professional translator, and finally reviewed and translated back into English by bilingual speakers.

A pilot test was conducted before sending the survey to four mental health professionals for face validation. The pilot testing was done with 30 HCPs to ensure that the questionnaire was clear, and then finally validated by six experts (psychiatrists, family physicians, and public health physicians) who agreed with the pilot's results. Cronbach's alpha for internal consistency is 0.85. Data confidentiality was guaranteed. HCPs completed and submitted the questionnaire with informed consent.

The data were gathered using a self-administered online Arabic questionnaire, as it's the first language in SA and the main language for all the HCPs. The questionnaire was constructed from three main parts:

1. The demographics, work-related traits, and personal medical histories of the studied healthcare providers.
2. The collected data on caffeine consumption (various sources, doses, and context of its consumption, including locations, times, and weekly expenditure on caffeine products) are based on the previous studies[21,25,26].
3. The application of the DSM-V to evaluate the impact of caffeine consumption diagnosed four caffeine-related disorders: caffeine intoxication, caffeine-induced anxiety disorder, caffeine-induced sleep disorder, and caffeine-related disorder not otherwise specified (NOS)[17].

Statistical Analysis

SPSS [v. 22 (IBM Corp., Armonk, NY, USA)] was used to code and analyze the collected data at a predetermined level of significance (p-value < 0.05). Quantitative data were summarized as mean, median, standard deviation (SD), and range, and was analyzed using Mann-Whitney U and Student t-tests. Qualitative data were summarized as frequency (F) and percentages (%) and were analyzed using the Chi-square test. While the association between two continuous variables was done by the person coefficient correlation (PCC).

Results

94.3% of the 600 HCPs studied used caffeine, and 270 (47.3%) were caffeine dependent. The mean age of the recruited HCPs was 34.9 years and 8.6 SD, with 407 (67.8%) females, 414 (69.0%) married, 483 (80.5%) Saudi, 492 (82.0%) non-smokers, and 503 (89.0%) having no chronic diseases. There was no statistically significant difference ($p > 0.05$) between caffeine consumption and all the studied demographic variables (Table I).

With regards to the rate of the most used sources of caffeine per week, in descending order, they were coffee (202; 35.7%), tea (140; 24.7%), chocolate (68; 12.0%), rapid-made coffee, and soda soft drinks. On the other hand, the least frequently consumed CDs were, in descending order, energy drinks and decaffeinated coffee. The median daily caffeine consumption was 600.1 mg and the mean±SD equal 445.9±398 mg. The average (median and range) of the weekly expenditure on caffeine products was about 220 Saudi Riyals (SR) and ranged from 0 to 1,000 SR (Table II).

Caffeine consumption was most common at work (271; 45.2%), followed by at home (221; 36.8%), and was higher in the morning (444; 78.4%) than at night (306; 54.6%) (Figures 1 and 2).

According to the DSM-V caffeine dependence criteria, (270; 47.7%) of caffeine-user HCPs developed dependence, and (380; 67.1%) reported addiction symptoms (Table III). The most positive effects mentioned by the recruited caffeine-user HCPs were feeling active, confident, and happy (Table IV). On the other hand, the reported symptoms of caffeine intoxication, in descending order, were anxiety, irritability, nervousness, and gastrointestinal and sleep disorders.

The recruited caffeine-user HCPs reported also the following side effects: sleep disturbances, stomach problems, cardiac symptoms, and anxiety in 60%, 54%, 47%, and 30%, respectively, in decreasing order of severity (Table V).

All the reported caffeine effects (both positive or negative) were significantly *($p<0.05$)* negatively and inversely correlated with the total amount of caffeine consumed per day except for mood and physical activity. Working hours showed a fairly negative and significant ($p=0.03$) correlation with their effect on mood and mental effects. Caffeine dependence is significantly associated with age ($p=0.03$) (Table VI). There was no statistically significant difference between sex and caffeine's effects except in mood and negative effects; its effect was significantly *($p=0.04$)* higher in men than females (Table VII).

Discussion

Caffeine is the most commonly used substance worldwide. Neuroenhancement is a topic that garners interest from both the general public and

Table I. The relationships between the caffeine consumption and the following demographic variables.

		Consume caffeine		
	Total No = 600	Yes No = 566 (94.3%) F (%)	No No = 34 (5.6%) F (%)	p
Age (y) mean ± SD	34.9 ± 8.6	34.9 .7	34.3 ± 7.7	0.98
Sex				0.09
Females	407 (67.8)	388 (68.6)	19 (55.9)	
Males	193 (32.2)	178 (31.4)	15 (44.1)	
Marital status				0.62
Widow	15 (2.5)	13 (2.3)	2 (5.9)	
Single	145 (24.2)	136 (24.0)	9 (26.5)	
Married	414 (69.0)	393 (69.4)	21 (61.8)	
Divorced	26 (4.3)	24 (4.2)	2 (5.9)	
Nationality				0.05
Saudi	483 (80.5)	453 (80.0)	30 (88.2)	
Non-Saudi	117 (19.5)	113 (20.0)	4 (11.8)	
Specialty				0.87
Nurse	173 (29.0)	161 (28.4)	13 (38.2)	
Pharmacy	26 (4.3)	24 (4.2)	2 (5.9)	
Physicians	124 (20.7)	118 (20.8)	6 (17.6)	
Public health technician	83 (13.8)	77 (13.6)	5(14.7)	
Applied science specialist	101 (16.8)	99 (17.9)	2 (5.9)	
Dentist	58 (9.7)	54 (9.5)	4 (11.8)	
Others	34 (5.7)	30 (5.6)	2 (5.9)	
Working hours				-----
Median (range)	8 (4-16)	8 (6-16)	8 (4-16)	
Smoking status				0.79
Not smoker	492 (82.0)	464 (82.0)	28 (82.4)	
Ex–smoker	24 (4.0)	22 (3.9)	2 (5.9)	
Smoker	84 (14.0)	80 (14.1)	4 (11.8)	
Having chronic diseases				0.16
No	503 (89.0)	478 (84.5)	26 (76.5)	
Yes	62 (10.9)	88 (15.5)	8 (23.5)	
Average weekly cost in SR (Saudi Riyal)	Median (mean ± SD)	220 (78.7 ± 100.9) range	(0-1,000)	

Table II. The sources, and amount of the caffeine consumption.

	1 cup/bar F (%)	2-3 cup/bar F (%)	> 3 cup/bar F (%)	No use F (%)
Coffee (125 ml/cup)	115 (19.2)	61 (10.2)	16 (2.7)	374 (66.1)
Espresso (30 ml/cup)	110 (18.3)	38 (6.3)	15 (2.5)	403 (71.2)
Rapidly made coffee (125 ml/cup)	227 (37.8)	61 (10.2)	26 (4.3)	252 (44.5)
Decaffeinated coffee (125 ml/cup)	64 (11.3)	18 (3.2)	4 (0.7)	480 (84.8)
Arabic coffee (80 ml)	174 (30.7)	159 (28.1)	112 (19.8)	121 (21.4)
Turkish coffee (80 ml)	185 (32.7)	55 (9.7)	22 (3.9)	304 (53.7)
Tea (150 ml/cup)	223 (37.2)	131 (23.1)	79 (14.0)	133 (23.5)
Iced tea (300 ml/cup)	52 (9.2)	15 (2.7)	1 (0.2)	498 (88.0)
Hot chocolate drinks (150 ml/cup)	110 (19.4)	30 (5.3)	8 (1.4)	418 (73.9)
Sodas and soft drinks (330 ml)	173 (30.6)	51 (9.0)	27 (4.8)	315 (55.7)
Diet soft drinks (330 ml)	91 (15.2)	23 (4.1)	9 (1.6)	443 (78.3)
Energy drinks (330 ml)	59 (10.4)	18 (3.2)	5 (0.9)	484 (85.5)
Chocolates (30 gm)	231(38.5)	82 (13.7)	36 (6.0)	217 (38.3)
White chocolates	93 (16.4)	31 (5.5)	6 (1.1)	436 (77.0)
Dark chocolates (30 gm)	164 (29.0)	53 (9.4)	13 (2.3)	336 (59.4)
Average daily caffeine consumption Median (mean ± SD)		600.1 (445.9 ± 398.7)		

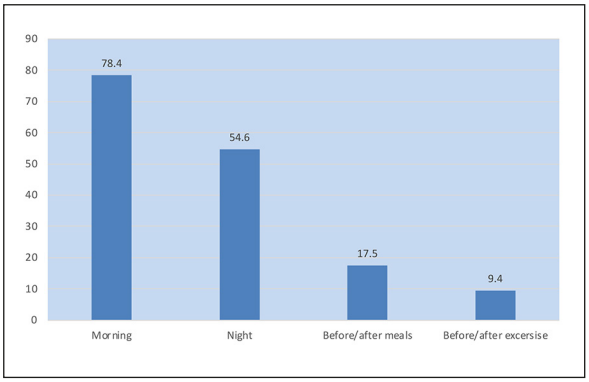

Figure 1. The most common times to drink caffeine among HCPs.

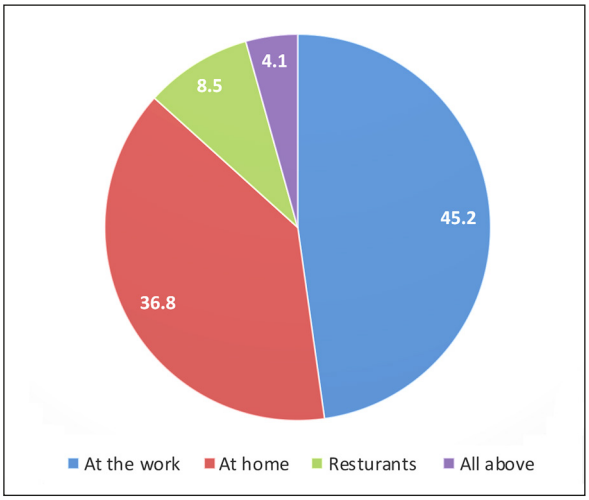

Figure 2. The most common sites for caffeine consumption among HCPs.

the scientific research community. However, the consumption of caffeine as a pharmacological neuroenhancer by HCPs is mostly unknown[27]. This work represents the first Saudi cross-sectional study to assess caffeine consumption among HCPs in KSA in terms of how commonly it was used, and what effects it had. Caffeine consumption is prevalent among HCPs in KSA, showing a rate of (566; 94.4%), which is higher than what was reported in the United Arab Emirates, where 86% of university students consume caffeine[28]. This could be attributed to an increase in caffeine consumption with age[29].

The high frequency of caffeine consumption among HCPs occurs on a daily basis. This is due to caffeine's beneficial effects on physical, mental, emotional, and spiritual well-being. It also has an immediate effect on the body, reaching peak levels in 30 to 60 minutes and having a half-life of 3 to 5 hours[29].

With regards to the daily amount of caffeine consumption among HCPs, the findings revealed that the median/(mean±SD) daily caffeine consumption was 600.1/(445.9±398.7) mg. This is worrisome because the recommended dose is 180 mg/day while the safe dose for a healthy adult is 400 mg per day. On the other hand, it is much higher (by at least twice) than in other studies involving various populations, such as soldiers (285 mg/day), psychiatric patients (281± 325 mg/day), office workers (205.7±34.9 mg/day), the general population (164.5±0.9 mg/day and 193 mg/day), adolescents (241.3±25.9 mg/day and 91.5 mg/day), and children (76.1±6.3 mg/day. This could be due to HCPs in this study having a higher level

Table III. Adopted DSM-V substance dependence criteria for caffeine among caffeine users.

Variable	F (%)
Caffeine withdrawal and tolerance (No = 566)	
Tolerance	
Feel tired when don't eat the usual amount of caffeine.	380 (67.1)
Withdrawal	
Feel a strong desire if I do not take the usual amount.	392 (69.3)
Need to take caffeine every day (CDs craving)	417 (73.67)
Hard to start the day without caffeine.	367 (64.84)
Worried when stop taking caffeine.	284 (50.2)
Unable to complete day-to-day tasks without caffeine (addiction)	294 (51.9)
Had headaches when stop caffeine.	353 (62.36)
Meet the DSM-IV substance	
Dependence criteria	270 (47.7)
Addiction	345 (60.9)
Self-assessment of caffeine withdrawal median (mean± SD)	24 (25.3 ± 13.2)

Self-assessment (Since 0 = does not apply, 10 applies perfectly).

Table IV. The positive effects of caffeine among HCPs caffeine users.

The positive effects of caffeine	F (%)
Caffeine effects on the mental activity	
Makes me more attentive.	438 (77.38)
Reduces the feeling of drowsiness.	451 (79.7)
Makes me feel active.	453 (80.0)
Helps me work for long periods.	423 (74.73)
Motivates me to work more.	428 (75.6)
The total mental activity score; median (mean ± SD) (range)	18 (18.9 ± 11.38) (5-44)
Caffeine effects on the appetite	
Discourages the hunger.	349 (61.7)
Helps avoiding eating more than needed.	330 (58.3)
Allows me to skip meals.	316 (55.8)
Reduces the appetite.	329 (58.1)
Helps controlling weight.	250 (44.2)
Self-assessment of caffeine effect on the appetite; median (mean ± SD) (range)	18 (19.29±10.93) (5-45)
Caffeine effects on mood	
When I am in caffeine, I am happy.	410 (72.4)
Feel more confident when taking caffeine.	277 (48.93)
Improves the mood.	446 (78.8)
Makes kinder.	333 (58.8)
Taking caffeine, it is more social.	309 (54.6)
Self-assessment of caffeine effect on mood; median (mean ± SD) (range)	17 (18.3 ± 11.00) (5-45)
Caffeine effects on physical activity	
Improve physical performance.	277 (48.9)
Helps doing physical activity for long periods.	262 (46.3)
Better physical activity after caffeine intake	270 (47.7)
Self-assessment of caffeine effect on physical activity; median (mean ± SD) (range)	9 (10.5 ± 6.5) (3-27)

Self-assessment Likert scale (0 = not apply, 10 applies perfectly).

of perceived stress and workload responsibilities, as caffeine has been shown to help with stress reduction and performance[27-30].

Determinants of Caffeine Consumption Among Hcps

Although we found that there was no statistically significant ($p > 0.05$) difference between caffeine consumption and all the studied demographic variables, there was a slightly higher prevalence of caffeine use among smokers or ex-smokers, and people married to HCPs (94.9%). This may be because all over SA, there are national anti-smoking clinics that treat people who use tobacco with the global standard protocol. Similar results reported that there was no evi-

Table V. The negative effects of caffeine among HCPs caffeine consumption.

The negative effects of caffeine	F (%)
Caffeine induced anxiety disorder.	
Easy irritability after taking coffee.	190 (33.6)
Anxious after minimal amount of coffee	186 (32.9)
Makes me easy stimulated anger.	174 (30.7)
Makes me nervous	157 (27.7)
Caffeine related disorder not otherwise specific	
Irregular heart rate.	271 (47.9)
Stomach disorders	311 (54.9)
Makes me sweat	165 (29.2)
Caffeine induced sleep disorders.	
When I take caffeine late, I get insomnia.	363 (64.1)
I have trouble sleeping with caffeine.	360 (63.7)
Caffeine intake all the time affects my sleep	302 (53.4)
The total negative effect score	
Median (mean ± SD) (range)	19 (21.02±12.19) (7-63)

Table VI. The correlation the age and working hours and the caffeine effects.

Caffeine effect	Age(y) r (p)	Working hours r (p)	Total caffeine consumption mg/day r (p)
Physical activity	0.04 (0.47)	-0.05 (0.47)	-0.11 (0.07)
Sleep disturbance	-0.07 (0.23)	-0.04 (0.47)	-0.52 (< 0.001*)
Mood	0.05 (0.40)	-0.14 (0.03*)	-0.09 (0.28)
Appetite	-0.13 (0.06)	-0.04 (0.59)	-0. 39 (< 0.001*)
Mental effects	-.04 (0.48)	-0.17 (0.03*)	0.61 (< 0.001*)
Negative effects	-0.05 (0.64)	-0.04 (0.12)	0.71 (< 0.001*)
Dependence	-0.16 (0.02*)	0.04 (0.59)	0.83 (< 0.001*)

*There is statistically significant difference.

dence for causal effects of smoking on caffeine use, or vice versa, among Dutch and British individuals[31,32].

Caffeine use and sex were statistically insignificantly correlated, but caffeine use was slightly more prevalent among women (388; 68.6%). This may be attributed to SA's cultural and entertainment factors. Moreover, its effective role in lowering the levels of adiposity in women has been shown, as it has been reported that females aged 20-44 years who drank two or three cups of coffee per day had the lowest levels of adiposity, and women aged 45-69 years who drank four or more cups had a 4.1% lower adiposity. This may be attributed to the increased body temperature through coffee administration which increases the metabolic rate in randomly assigned individuals. Furthermore, regular drinking of hot tea was associated with reduced fat amounts[33-35]. On the contrary, another systematic review discovered that men daily drink more coffee than women (2.4 cups of coffee, compared with 1.9 cups in women) and that only 32% of women drink coffee, compared to over 50% of men[37].

Surprisingly, Saudis (453, or 80.0%) consumed more caffeine than non-Saudis. This can be explained by the fact that coffee has historically held great value in Arab culture and is commonly served as a beverage at social gatherings, weddings, and other important events. In an Arab household, the "dallah," or Arabic-style coffee pot, is always present and served many times in tiny Arabic mugs. This contradicts previous results that showed that immigrant stresses could be a factor in rising caffeine consumption among those immigrants, which is also in agreement with another study[36] that reported that immigration-related stress was significantly associated with a rise in the alcohol intake, and caffeine consumption may also exhibit a similar pattern.

Furthermore, HCPs who reported caffeine intoxication also had significantly higher levels of caffeine consumption, as the more caffeine they consumed, the more symptoms they experienced. Similarly, a study[39] done in the United States found that drinking too much caffeine can cause manifestations of caffeine intoxication.

Among the recruited caffeine-user HCPs, the average caffeine intake was 370 mg/day, which is higher than the recommended 180 mg/day in adulthood for the general population[31] mainly in the form of coffee. Other studies[38] showed that adults mostly drink coffee and tea, while chil-

Table VII. The relationship between sex and the following the caffeine effect on the following domains.

	Females No = 407 F (%)	Males No =193 F (%)	p
Physical activity	155 (38.1)	108 (55.9)	0.25
Sleep	177 (48.5)	91 (47.2)	0.09
Mood	156 (38.3)	183 (43.0)	0.04*
Appetite	142 (34.9)	63 (32.6)	0.89
Mental	247 (60.7)	119 (61.7)	0.09
Negative effects	59 (14.5)	30 (25.6)	0.04*
Median (mean ± SD)	17 (19.1 ± 11.1)	22 (24.6 ± 13.3)	
Dependence	159 (39.1)	67 (34.7)	0.59
Median (mean ± SD)	24 (24.9 ± 13.4)	25 (26.0 ± 12.6)	

*There is statistically significant difference.

dren and teens mostly drink carbonated drinks, and hot chocolate, both of which have much less caffeine[24,38]. Most dietary caffeine is consumed as a beverage.

In our study, about 10% of people said they drank energy drinks two to four times a week. This is a higher percentage than what other studies[39] have found in SA, where only 5.1% of the population drank energy drinks two to four times a week. It is also lower than what Reid et al[29] found in a national online survey in Canada in 2016, where 15% of youth and young adults stated consumption of energy drinks.

It is worth mentioning that (270; 47.7%) of the recruited caffeine-user HCPs met the DSM-V caffeine dependence criteria, which is higher than the percentage reported among the general population (30%). Taking about 100 mg of caffeine per day (one cup of coffee) can lead to physical dependence and can cause withdrawal symptoms such as headaches, lethargy, depression, and extreme irritability. Johns Hopkins neurology professor Roland R. Griffiths believes caffeine withdrawal should be considered a psychological disorder, and he says that 50% of regular coffee drinkers start having withdrawal symptoms 12-24 hours after they stop drinking caffeine[18].

A larger proportion (47.7%) of the recruited caffeine-user HCPs reported more caffeine dependence and addiction signs than the general population: tolerance (380, 67.1%) *vs.* 8%; CDs craving (417, 73.67%) *vs*. 34.7%; and withdrawal symptoms (284, 50.2%) *vs.* 26%. In addition to the behavioral reward effects of caffeine, which explain the psychological dependence on caffeine with the accompanied reinforcement, caffeine antagonizes the adenosine A1 receptor, a mechanism that blocks endogenous adenosine with subsequent behavioral stimulant effects and also removes the negative modulatory effects of adenosine at dopamine receptors. Moreover, paraxanthine, the primary metabolite of caffeine in humans, produces increased locomotor activity, as well as increases extracellular levels of dopamine through a phosphodiesterase inhibitory mechanism[40]. Increased dopamine release in the nucleus acumens may be a specific neuropharmacological mechanism that explains how caffeine can make people addicted to it[41]. Up-regulation of the adenosine system following chronic caffeine administration appears to be a neurochemical mechanism underlying caffeine tolerance and withdrawal syndrome with increased functional sensitivity to adenosine during caffeine abstinence and the development of caffeine withdrawal's behavioral and physiological effects[27,42].

There was an indirect significant correlation between age and dependence of r = 0.16 (p= 0.02*) where these dependence effects are more pronounced in older adults because their bodies process caffeine more slowly[35]. Coffee has more caffeine than most drinks[43]. Caffeine dependence is significantly affected by age.

Positive Effects of Caffeine Consumption

Caffeine had positive effects on HCPs' mental activity, mood, and appetite. Caffeine users agreed that it improved their academic performance, especially their ability to stay awake and alert. This backs up the findings that neuroenhancement is a common reason for using pharmaceuticals on French and American college campuses. So that it can be used for recreational purposes and not exclusively for cognitive enhancement[27]. Caffeine can cross blood-brain barriers, permitting it to reach the brain and exert its effects *via* adenosine receptors. Caffeine alters the expression of proteins such as BDNF and CREB in the hippocampus and cortex, leading to alterations in learning and memory processes[46].

Negative Effects of Caffeine Consumption

Although caffeine is "generally recognized as safe," or GRAS by the Food and Drug Administration (FDA) therefore is not regulated as a food additive[30], however, the present work showed that consumption of caffeine has been reported to cause the following negative effects, in descending order: (60%) sleep disruption; (54%) stomach problems; (47%) irregular heart rate; and (30%) anxiety. This constellation of symptoms is referred to as "caffeinism," which is clinically indistinguishable from severe chronic anxiety and typically occurs with high daily intake[24]. Meredith et al[18] found that teens who used drugs had fewer negative effects, whereas 36%, 9%, 16%, 1%, and 0% of the sample reported sleep disorders, anxiety, stomach problems, and heart problems, respectively.

Sleep disturbance was the most commonly reported negative effect by more than 60% of the recruited caffeine-user HCPs which agrees with a previous study[45] stating that 54.6% of Americans commonly consume caffeine at night, and that consuming caffeine six hours before bedtime reduces the total sleep time by one hour and delays

the timing of your body clock. Similar findings by Alfawaz et al[32] indicate that sleep disturbance is a common problem among HCPs, with caffeine consumption being one of the main causes. Meanwhile, in another study[45], 30% of HCPs were reported to have negative effects like depression and anxiety, mostly because of caffeine's potential to make people anxious.

These negative effects of caffeinism (insomnia, anxiety, cardiovascular manifestations, and gastric upset) can be attributed to increased catecholamine levels *via* presynaptic adenosine A1 receptor antagonism (and possibly blockade of the adenosine A1 receptor of the adrenal medulla) and beta-1-adrenergic agonism *via* increased catecholamines, which ultimately results in increased levels of cyclic adenosine monophosphate (cAMP) *via* adenylyl cyclase activation. These increased levels of cAMP are further enhanced by the inhibition of phosphodiesterase. It has also been suggested that caffeine might work by binding to and activating calcium-release channels (i.e., the ryanodine receptors, or RyRs) in skeletal muscle, cardiac muscle, and neuronal tissue, causing calcium to leak out of the cells. This is unlikely to happen with normal caffeine consumption[39].

The number of remaining negative findings was high, constituting a considerable portion of the studied sample, with the reported prevalence of the negatives at about 30%. A thorough review found that healthy adults who drink up to 400 mg of caffeine every day for a long time do not experience negative effects on their heart health, calcium balance and bone health, behavior, cancer risk, or male fertility[45].

Limitations

The fact that this study was conducted exclusively online restricts the generalizability of the findings and may lead to selection bias with regards to respondents, 67.8% of whom were female, along with nurses (29%), and public health technicians (20%). The sample includes more than 22 nationalities, with different transcultural factors that make the prevalence or intensity of caffeine consumption more comprehensive. Moreover, we only studied HCPs working in one country, and the frequency of consumption may differ in other countries. Furthermore, including a clinical sample could have provided additional insight into caffeine's role in the scenario of possible caffeine-induced psychiatric disorders and toxic manifestations.

Strenghts

The relatively large sample of HCPs working in governmental health care and settings in urban and rural areas represents a strenght of this study. Also, a detailed survey that looks at the different types, amounts, and rates of caffeine consumption, and the expected clinical manifestations of dependence and addiction. These might give us more information about how demographic factors affect how often people drink caffeine and develop symptoms and signs of toxicity.

Recommendations

Caffeine-containing products consumption requires special consideration, including:

1) Further research is needed to provide evidence-based recommendations and study the relationship between various demographic factors and caffeine consumption and toxicity in greater depth. A multicenter study using the recently released DSM-V-TR in April 2022 in various countries and among different occupations would provide better evidence.
2) To decrease the frequency of the negative/toxic effects of caffeine, we recommend the following:

   I. Public health education campaigns, especially for HCPs, about the safety of caffeine-containing products and their potentially harmful effects; avoiding caffeine in the late afternoon and evening; and avoiding powdered pure caffeine, using the American Academy of Sleep Medicine (AASM)[46] guidelines as a teaching tool.

   II. Caffeine consumption should be limited to 300-400 mg per day. Caffeine Safety Limits: use this link to calculate your safe daily dose of caffeine; (caffeineinformer.com). For detailed information about the average caffeine content per cup of drink, check the supplementary material or visit this web page. The knowledge of caffeine content in foods and beverages is to be updated. HCPs with cardiovascular diseases should avoid high levels of caffeine consumption[38].

   III. Further studies about the safety of caffeine consumption among vulnerable groups, such as pregnant and lactating women, should be conducted. Caffeine can cross both the placental and blood-brain barriers[47].

   IV. At the policy level, we recommend showing the amount of caffeine in a drink by being added to the ingredient on the drink's label.

Conclusions

According to this study, caffeine is widely consumed among governmental HCPs in KSA. The frequency of caffeine dependence and addiction is high as well. Arabica coffee is the most consumed coffee type. In addition, the amount of caffeine consumed is significantly and directly correlated with the severity of caffeine intoxication symptoms. Caffeine had the greatest positive effects on mental health and mood, while its most negative effects are on sleep and the digestive system. Except for mood and physical activity, caffeine effects were significantly inversely correlated with the total amount of caffeine consumed per day. Working hours showed a fair, significant indirect correlation with its effect on mood and mental effects. Caffeine dependence is significantly affected by age. Except for mood and bad effects, there was no statistically significant difference

Conflict of Interest
The Authors declare that they have no conflict of interests.

Acknowledgements
We would like to thank all the HCPs who participated in this study. Special thanks to the General Administration of Clinical Health Education, Ministry of Health, Saudi Arabia, for their unlimited support in the distribution of the survey to conduct this study. Special thanks to Dr. Raghda Hamed Deraz at the Department of Forensic and Toxicology, Zagazig University, Egypt, for her contribution to the study and language editing.

Availability of Data and Materials
The datasets used and/or analysed during the current study are available from the corresponding author upon request to dr_samar11@yahoo.com.

Funding
Self-funded.

Ethics Approval
King Fahad City IRP exempt type approved this study, IRP Log Number 19-132E.

Informed Consent
All participants provided electronic informed consent after clarification of the goals, data confidentiality, voluntary participation, and withdrawal.

Authors' Contribution
SA, DA, AF, JS, FA and GH came up with the idea for the study, wrote the protocol, and designed the data. The data collection tools are DA, FA, AF and GH. SA performed the statistical analysis and drafted the manuscript. ME,NZ contributed to the writing of the "Discussion" section and provided final approval of the manuscript. All authors reviewed, edited, and approved the manuscript.

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