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Antifungal prescribing pattern and attitude towards the treatment of oral candidiasis among dentists in Jordan

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Aim: The aim of this study was to evaluate the attitude of Jordanian dentists towards the treatment of oral candidiasis and their current antifungal prescribing habits, shedding more light on the possible influence of their socio-professional factors on the pattern of prescribing and practice. **Methods:** A structured validated questionnaire was developed and tested; it was then emailed to a random sample of 600 Jordanian dental practitioners during the period of this cross-sectional survey. The questionnaire recorded practitioners' personal details and their attitude and prescribing of antifungal therapy for oral candidiasis. Statistical significance was based on probability values of <0.05 and was measured using the chi-square and Fisher's exact tests. Multiple logistic regression analysis was used to analyse the influence of respondents' socio-professional factors on their attitude towards oral candidiasis. **Results:** Of the 423 questionnaires returned, only 330 were included. The attitude of respondents was significantly influenced by their experience [odds ratio (OR) = 0.14; $P < 0.001$] and workplace (OR = 4.70; $P < 0.001$). Nystatin was the most commonly prescribed antifungal agent (78.2%), followed by miconazole (62.4%), which was prescribed for topical use. Systemic antifungals were prescribed by 21.2% of respondents, with a significant ($P < 0.05$) association with the country in which their qualification was obtained. **Conclusion:** The attitude towards the treatment of oral candidiasis is much better among the least-experienced dentists working in private practice. Nystatin and miconazole are the most popular choices of antifungal agents among Jordanian dentists.

Key words: *Antifungal prescribing, attitude, Jordan, dentists*

INTRODUCTION

Candida albicans is a normal finding in the oral cavity of the healthy population[1]. However, *C. albicans* has the potential to become problematic and pathogenic when its levels are increased or during exposure to single or multiple local and systemic factors, including environmental or host-dependent factors[2–8]. Oral candidiasis is the commonest human fungal infection[9], and candidal infections are currently by far the most commonly recorded fungal infections in patients with human immunodeficiency virus (HIV) and acquired immune-deficiency syndrome (AIDS)[10]. A recent study[11] on Jordanian infants reported significant production of putative virulence enzymes of phospholipase and protease by most of the oral and rectal *C. albicans* isolates. Hence, if this infection is left untreated, it can lead to poor nutritional intake, speech impairment and prolonged recovery[9,12].

Epidemiological reports have indicated some changes in fungal infections between 2004 and 2014[13], namely a marked increase in their incidence, particularly those caused by *Candida* species[10]. Many key risk factors have contributed to the increasing incidence of opportunistic infections caused by *Candida* species, including: an increase in the incidence of diabetes mellitus; an increase in average life expectancies; the use of certain medications, such as broad-spectrum antibiotics and immunosuppressants; and certain immunodeficiency states, such as HIV positivity[14]. Furthermore, a high incidence of invasive *Candida* infections has been reported in intensive care unit (ICU) patients[15,16] following procedures such as abdominal surgery, organ transplantation and the

placement of a central venous catheter. Hence, the use of different topical and systemic antifungal treatment modalities has been significantly increased. Unfortunately, antifungal drugs may be used inappropriately and this contributes to the worldwide increase in antifungal resistance, particularly to the group of azoles[17,18]. Also, resistance to antifungal therapy may be responsible for a wide range of adverse outcomes, including non-responsive infections, exposure of patients to ineffective medications and higher treatment costs[19].

Generally, the patient's immune state and type of pathology have to be considered when antifungal drugs are prescribed for the treatment of oral candidiasis. Topical treatment should be the first choice in immunocompetent patients, whereas systemic therapy is used as prophylaxis or for treatment of immunocompromised patients and for lesions not responding to topical treatment[20]. Furthermore, an Expert Panel of the Infectious Diseases Society of America has recently prepared guidelines[16] for the management of patients with invasive and mucosal candidiasis, and recommended the treatment of oropharyngeal candidiasis according to the severity of disease; topical therapy with clotrimazole or nystatin for mild infections; fluconazole for moderate-to-severe infections; and itraconazole, voriconazole, posaconazole or amphotericin B suspension for refractory infections. However, systemic treatment, unlike topical treatment, has the potential for greater adverse systemic effects, such as hepatotoxicity and interactions with other drugs[21]. Thus, the combination of topical and systemic treatment modalities would sometimes be advantageous for reducing the dose or duration of the systemic treatment[22].

Antimicrobials are among the drugs most frequently prescribed by dentists[23]. Many studies have been conducted to investigate dental antibiotic prescribing[23–25]. In Jordan, where this study was conducted, dentists' antibiotic-prescribing practices were found to be less than ideal. Jordanian dental specialists had a tendency to overprescribe antibiotics[23], and a substantial proportion of dentists had a tendency to prescribe long courses of antibiotics, as well as to prescribe broad-spectrum antibiotics[23,25]. However, studies examining the attitude of dentists towards the treatment of oral candidiasis are scarce[21] and the studies that are available show inconsistent methods in evaluating the influence of their socio-professional factors. A review of literature published in the last 20 years showed that only three studies investigated the attitude of dentists towards the treatment of oral candidiasis and their antifungal-prescribing habits: one was conducted in the USA, 20 years ago[26]; one was conducted in the UK, 10 years ago[21]; and a recent study was conducted in 2010 in Spain[27]. As far as we know, no such studies have been conducted in a developing country such as Jordan.

The aim of this study was to evaluate the attitude of Jordanian dentists towards the treatment of oral candidiasis and their current antifungal-prescribing habits, shedding more light on the possible influence of their socio-professional factors, including gender, workplace (private or public), and year (new or old graduates) and country (Jordan or other) of qualifications.

MATERIALS AND METHODS

This cross-sectional questionnaire-based survey was conducted during the period 7 January 2013 to 31 August 2013. A constructed questionnaire was developed for the purpose of this study. It was written in English, recorded participants' socio-professional details (including age, gender, workplace, professional practice and year and country of first degree qualification), their current prescribing habits of the available antifungal drugs approved to treat oral candidiasis in Jordan and their attitudes towards the treatment of oral candidiasis.

The initial draft of the questionnaire was prepared and included some items used in previous studies[21,26,27]. The questionnaire was piloted and tested for clarity and simplicity of the items by being hand distributed to 10 dentists. Based on their comments, the questionnaire was modified and adjusted to make it easier for participants to understand and answer. The final questionnaire was then distributed to 20 participants. The reliability of the questionnaire was tested by asking the 20 participants to answer the questionnaire on another occasion, 1 week later. Kappa statistics were 0.91–0.95 for the items, indicating high reliability of the questionnaire.

The final form of the questionnaire (*Figure 1*) was sent by email and comprised the questionnaire as a separately attached file, and a cover page describing the study aims and objectives precisely, so that the survey was not interpreted as a monitoring exercise on the quality of care, which, if so, could bias the respondents' answers. In addition, in the final paragraph of the cover page, practitioners were informed that 'completing and returning the questionnaire is considered as written consent and agreement of participation'. A list of 1,200 dental practitioners, who were practicing dentistry over the period of the study, and for whom email access and other contact details were available, were obtained from the Jordan Dental Association (JDA). The questionnaire was emailed to a sample of 600 Jordanian dentists, randomly and systematically selected by choosing every second practitioner on the same list. Only two emails were sent: the first in January 2013; and the second, which was a follow-up email, approxi-

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Please fill in the following questionnaire:

1. Socio-professional details:

- **Age:----------** **Gender:** ☐ M ☐ F
- **Professional practice:**
  - ☐ GDP (General dental practitioner)
  - ☐ SDP (specialist dental practitioner):
    - ☐ Oral surgery ☐ Periodontology ☐ Operative dentistry
    - ☐ Prosthodontics ☐ Orthodontics ☐ Paedodontics
    - ☐ Oral medicine
- **Workplace:**
  - ☐ Private Practice
  - ☐ Public Practice: ☐ Ministry of Health ☐ University Hospital ☐ Military Hospital
- **Year of first degree qualification**
  - ☐ 2001-2010 ☐ 1991-2000 ☐ Before 1991
- **Country of first degree qualification:**
  - ☐ Jordan ☐ Non-Jordan

2. Attitudes towards oral candidiasis:

- **Number of cases diagnosed per month**
  - ☐ 0-1 cases ☐ 2-3 cases ☐ ≥ 4 cases
- **What is your action following diagnosis of oral candidiasis?**
  - ☐ Refer to oral medicine specialists ☐ Treat by myself
- **Please tick the type(s) and the form(s) of the *approved* antifungal agent(s) you prescribe to treat oral candidiasis.**

Antifungal	Form
☐ Topical treatment	
☐ Systemic treatment	
☐ Nystatin: (topical)	❑ Pastille ❑ Oral suspension
☐ Amphotericin: (topical)	❑ Lozenges ❑ Oral Suspension
☐ Miconazole Oral Gel (topical)	
☐ Chlorhexidine: (topical)	❑ Adjunctive use ❑ Non-adjunctive use
☐ Fluconazole (systemic)	
☐ Other: ----------	
☐ Nil	

----------**THANK YOU**

Figure 1. The questionnaire.

mately 2 months later to non-responders who might not use their emails regularly or to responders who returned questionnaires with incomplete responses. The questionnaire was anonymous – patient's or respondent's identity or confidential information were not disclosed or requested by any question. This study was conducted in full accordance with the World Medical Association Declaration of Helsinki and was approved by the Ethical Research Committee of the Faculty of Dentistry, the University of Jordan.

The SPSS version 19.0 (SPSS Inc., Chicago, IL, USA) statistical software program was used for the statistical analysis. Descriptive statistics, frequency distributions and cross-tabulation were produced. Statistical differences between frequencies were measured using chi-square and Fisher's exact tests. Multiple logistic regression analysis was used to assess the influence of participants' professional details on their attitude towards the treatment of oral candidiasis. $P < 0.05$ was considered significant.

RESULTS

A total of 600 questionnaires were emailed to dental practitioners who were practicing dentistry in Jordan during the time period of this survey, and 423 dentists [general dental practitioners (GDPs) and specialist dental practitioners (SDPs)] responded and returned completed questionnaires (70.5% response rate). Of the 423 questionnaires returned, only 330 (78%) were included in the statistical analysis. The remaining 93 (22%) questionnaires were excluded: eight (1.9%) had a few questions that were not answered; 22 (5.2%) were returned by retired respondents; and 63 (14.9%) were returned by respondents who had postgraduate qualifications (i.e. were SDPs) in maxillofacial surgery (3.8%), oral medicine (1.9%), orthodontics (1.7%), operative dentistry (1.9%), prosthodontics (2.8%), pedodontics (0.9%) and periodontics (1.9%). Therefore, the basis for undertaking the percentage results was considering questionnaires with completed answers for each single question and only for GDPs.

The mean age ± standard deviation (SD) of the 330 respondents included was 38.8 ± 10.0 [median (range): 37.0 (26.0–70.0)] years. There were 206 (62.4%) male respondents and 124 (37.6%) female respondents. The workplace for 194 (58.8%) respondents was private practice and for 136 (41.2%) was public practice – Ministry of Health (20%), university hospitals (9.7%) and Military Medical Services (11.5%). The majority of respondents (40.6%) graduated between 2001 and 2010, more than one-third (38.8%) graduated between 1991 and 2000, and the remaining 20.6% graduated before 1991. Lastly, the first degree qualification of 191 (57.9%) respondents was granted by Jordanian universities and by other countries for the remaining 139 (42.1%).

The participants reported the number of cases diagnosed with oral candidiasis each month in the last year; 0–1 cases were diagnosed by 185 (56.1%) respondents, 2–3 cases by 108 (32.7%) and more than three cases by the remaining 37 (11.2%). Therefore, the majority (88.8%) of dentists diagnosed a few cases of oral candidiasis (fewer than four) per month and only 11.2% diagnosed more than three. Male participants, those with Jordanian qualifications and those working in private practice diagnosed a higher number of cases ($P < 0.01$) compared with female participants, those with non-Jordanian qualifications and those working in public practice, respectively. Respondents' year of qualification was found to have a significant ($P < 0.001$) association with the number of cases diagnosed per month; the fewest number of cases diagnosed (none or one) was commonly reported by dentists who graduated in 2001–2010, two to three cases were commonly reported by dentists who graduated in 1991–2000 and the highest number of cases (more than three)

Table 1 Number of cases of oral candidiasis diagnosed each month by participating dentists, stratified according to socio-professional factors (gender, workplace and year and country of first degree qualification) ($n = 330$)

Socio-professional factors	Cases of oral candidiasis diagnosed per month				
	0–1 *n* (%)	2–3 *n* (%)	≥4 *n* (%)	Total *n* (%)	*P**
Gender					
Male	121 (65.4)	52 (48.1)	33 (89.2)	206 (62.4)	0.001
Female	64 (34.6)	56 (51.9)	4 (10.8)	124 (37.6)	
Total	185 (100)	108 (100)	37 (100)	330 (100)	
Workplace					
Private practice	100 (54.1)	64 (59.3)	30 (81.1)	194 (58.8)	0.010
Public practice	85 (45.9)	44 (40.7)	7 (18.9)	136 (41.2)	
Total	185 (100)	108 (100)	37 (100)	330 (100)	
Year of first degree qualification					
2001–2010	134 (72.4)	0 (0)	0 (0)	134 (40.6)	0.001
1991–2000	24 (13)	104 (96.3)	0 (0)	128 (38.8)	
Before 1991	27 (14.6)	4 (3.7)	37 (100)	68 (20.6)	
Total	185 (100)	108 (100)	37 (100)	330 (100)	
Country of first degree qualification					
Jordan	127 (68.6)	64 (59.3)	0 (0)	191 (57.9)	0.001
Other	58 (31.4)	44 (40.7)	37 (100)	139 (42.1)	
Total	185 (100)	108 (100)	37 (100)	330 (100)	

*Calculated using the chi-square test.

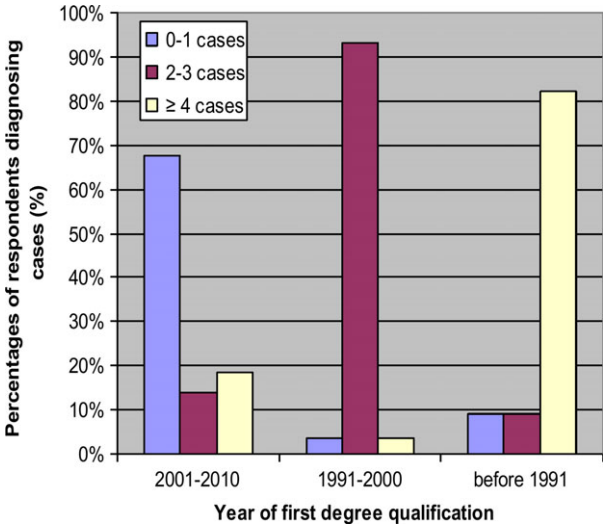

Figure 2. Cases of oral candidiasis diagnosed per month, according to the time period when the first degree qualification of respondents was obtained.

was commonly reported by older graduates (i.e. those who graduated before 1991) (*Table 1*, *Figure 2*).

When participants were asked of their action following diagnosis of oral candidiasis in the last year, 282 (85.5%) reported that they treated it by themselves, whereas 48 (14.5%) referred patients to oral medicine specialists. Multivariate regression analysis (*Table 2*) identified two socio-professional factors that were significantly associated with the action taken by respondents (referral *vs.* treatment): the year of first degree qualification [odds ratio (OR) = 0.14, $P < 0.001$] was significantly related to respondents' action of referral, suggesting that for every younger graduate (1991–2010) who referred patients, about 0.14 older graduates (before 1991) did so; and workplace differences were statistically significant (OR = 4.70, $P < 0.001$), in that respondents working in private practice tended to refer patients about five times more frequently than did those working in public practice. However, gender (OR = 0.68, $P = 0.33$) and country of first degree qualification (OR = 0.92, $P = 0.86$) did not affect respondents' action of referral.

The majority of respondents (85.5%) chose *one or more than one type and/or form* of antifungal in the last year. Prescription of topical antifungals was the choice of 292 (88.5%) respondents, whereas prescription of systemic antifungals was the choice of 70 (21.2%). Nystatin was the most commonly prescribed antifungal agent (78.2%), followed by miconazole (62.4%), amphotericin B (13.3%) and fluconazole (10.9%). The use of chlorhexidine was reported by 72.7% of respondents; 93.2% reported its use as an adjunct to conventional antifungal agents (*Table 3*). Pastilles were the most popular form of the available intra-oral preparations of nystatin, and were prescribed by 93% of those prescribing nystatin, whereas 45.7% used the oral suspension. With regard to the amphotericin B preparations available, the most commonly prescribed form was lozenges, which was used by 81.8% of those prescribing amphotericin, with the suspension form being prescribed only by 27.3%.

The respondents' choice of treatment of oral candidiasis with relation to their socio-professional details (including gender, workplace, and year and country of first degree qualification) is detailed in *Table 4*. Topical treatment was generally prescribed significantly ($P < 0.05$) more by male participants and younger graduates. By contrast, systemic treatment was generally prescribed significantly ($P < 0.05$) more often by respondents with Jordanian qualifications. However, one type of systemic treatment, fluconazole, was found to be ($P < 0.05$) prescribed significantly more often by male participants, younger graduates, respondents working in private practice and those with Jordanian qualifications.

Table 2 Logistic regression analysis of the influence of socio-professional factors on respondents' decision to refer patients to oral medicine specialists following a diagnosis of oral candidiasis(n = 330)

Variable	P*	Exp(B)(OR)	95% CI for Exp(B)	
			Lower bound	Upper bound
Gender (male *vs.* female)	0.331	0.683	0.316	1.475
Year of first degree (younger† *vs.* older‡)	**0.001**	0.140	0.049	0.402
Workplace (private *vs.* public)	**0.001**	4.696	2.358	9.351
Country of first degree (Jordan *vs.* other)	0.855	0.919	0.371	2.279

95% CI, 95% confidence interval; OR, odds ratio.
*Calculated using the Wald chi-square test.
†Graduated from 1991 to 2010.
‡Graduated before 1991.
Bold values indicate statistically significant at the 0.05 probability level (two-tailed).

Table 3 Respondents' choice of antifungal for treating oral candidiasis (n = 330)

Antifungal agents	Prescribe n (%)	Not prescribe n (%)
Topical treatment	292 (88.5)	38 (11.5)
Systemic treatment	70 (21.2)	260 (78.8)
Nystatin (topical)	258 (78.2)	72 (21.8)
Amphotericin (topical)	44 (13.3)	286 (86.7)
Miconazole Oral Gel (topical)	206 (62.4)	124 (37.6)
Chlorhexidine (topical)	240 (72.7)	90 (27.3)
Fluconazole (systemic)	36 (10.9)	294 (89.1)
Other	4 (1.2)	326 (98.8)

Table 4 Percentage differences in respondents' choice of treatment for oral candidiasis, classified according to socio-professional factors ($n = 330$)

Socio-professional factors	Prescribed treatment															
	Topical treatment		Systemic treatment		Nystatin		Amphotericin		Miconazole		Chlorhexidine		Fluconazole		Other	
	($n = 292$) *n* (%)	*P**	($n = 70$) *n* (%)	*P**	($n = 258$) *n* (%)	*P**	($n = 44$) *n* (%)	*P**	($n = 206$) *n* (%)	*P**	($n = 240$) *n* (%)	*P**	($n = 36$) *n* (%)	*P**	($n = 4$) *n* (%)	*P**
Gender																
Male ($n = 206$)	192 (93.2)	**0.001**	50 (24.3)	0.095	154 (74.8)	0.055	24 (11.7)	0.248	130 (63.1)	0.815	156 (75.7)	0.127	28 (13.6)	**0.046**	0 (0)	**0.019**
Female ($n = 124$)	100 (80.6)		20 (16.1)		104 (83.9)		20 (16.1)		76 (61..3)		84 (67.7)		8 (6.5)		4 (3.2)	
Workplace																
Private practice ($n = 194$)	175 (90.2)	0.293	39 (20.1)	0.586	146 (75.3)	0.138	12 (6.2)	**0.001**	120 (61.9)	0.818	146 (75.3)	0.258	36 (18.6)	**0.001**	4 (2.1)	0.146
Public practice ($n = 136$)	117 (86.0)		31 (22.8)		112 (82.4)		32 (23.5)		86 (63.2)		94 (69.1)		0 (0)		0 (0)	
Year of first degree qualification																
1991–2010 ($n = 262$)	242 (92.4)	**0.001**	60 (22.9)	0.182	214 (81.7)	**0.005**	36 (13.7)	0.842	175 (66.8)	**0.002**	207 (79)	**0.001**	36 (13.7)	**0.001**	4 (1.5)	0.585
Before 1991 ($n = 68$)	50 (73.5)		10 (14.7)		44 (64.7)		8 (11.8)		31 (45.6)		33 (48.5)		0 (0)		0 (0)	
Country of first degree qualification																
Jordan ($n = 191$)	171 (89.5)	0.491	52 (27.2)	**0.002**	155 (81.2)	0.139	16 (8.4)	**0.003**	132 (69.1)	**0.004**	155 (81.2)	0.001	32 (6.8)	**0.001**	4 (2.1)	0.141
Other ($n = 139$)	121 (87.1)		18 (12.9)		103 (74.1)		28 (20.1)		74 (53.2)		85 (61.2)		4 (2.9)		0 (0)	

*Fisher's exact test (two-tailed).
Bold values indicate statistically significant at the 0.05 probability level (two-tailed).

DISCUSSION

The term 'socio-professional details' used in this survey has been described in a recent study[27] and refers to the practitioner's age, gender, workplace, professional practice, and year and country of first degree qualification. To the best knowledge of the authors, the present study is the first to investigate the influence of different socio-professional factors of Jordanian dental practitioners on their treatment of oral candidiasis and their antifungal-prescribing habits. The influence of country of qualification has not previously been considered in the literature. In the present study, only GDPs were included in the statistical analysis because the number of specialists, particularly in oral medicine, was small relative to the number of GDPs and this small number of SDPs would make any statistical analysis invalid. Although Arabic is the mother language in Jordan, English is the official language used by the Jordanian Medical Council in its examinations for medical and dental practitioners seeking to obtain their professional permit. Hence, writing the questionnaire in English is justified and considered suitable for all the study population. A response rate of 70.5% in this study indicates that the current antifungal prescribing pattern and attitude towards the treatment of oral candidiasis among Jordanian dentists are reasonably represented.

Dental practitioners may need to treat immunocompetent and immunocompromised patients who have different types of oral candidiasis, and regular oral care of patients with HIV is no exception[28]. However, a previous study showed that a substantial proportion of Jordanian dentists are reluctant to treat this category of patients[29]. Management of oral candidiasis entails identification and correction of the predisposing factor, wherever possible, and selecting the antifungal agent that is suitable for the patient and the lesion. Furthermore, weighing the risks and benefits of use of a specific antifungal agent has to be taken into consideration[27,30]. In this regard, dentists should have sufficient knowledge on the diagnosis of oral candidal lesions to permit prescription of the appropriate antimicrobial therapy. However, it has been reported that this knowledge and attitude may be influenced by the practitioners' socio-professional factors, including gender, workplace and experience[21,27].

Regarding gender, a recent study reported that whereas the dental practitioners' gender had no association with the number of patients diagnosed with oral candidiasis, male gender did have a significant influence on prescribing habits, particularly of systemic antifungal agents[27]. This is in contrast to the significant associations found in the present study in which male dental practitioners tended to diagnose a greater number of cases of oral candidiasis and

preferred to prescribe topical antifungal agents. A possible explanation for this is that male dentists in Jordan work for longer hours, and have a heavier workload, than their female counterparts. Additionally, female dentists might have different educational experiences and practice opportunities that would influence their prescribing practices towards the less invasive topical treatment. This is consistent with other studies[31–35], which reported that female dentists are less likely to work full-time and tend to see fewer patients.

The experience of dentists is known to have a significant association with their attitude and prescribing habits, particularly of systemic antifungal agents[21,27]. This is in agreement with the significant association found in the present study that as the experience of the respondents increased, the more likely they were to diagnose and treat oral candidal infections. Additionally, younger participants in this study tended to employ topical treatment, in general, and sometimes prescribed fluconazole significantly more often than did older participants. The international trends of teaching dentistry have changed over the last two decades; older dental graduates used to study dentistry, especially the first 3 years, in medical faculties along with medical students. However, dentistry is a different discipline from medicine and this has repercussions for dental education. Consequently, older graduates tend to show a number of tendencies, such as the self-confidence to prescribe systemic treatment and a higher capability to diagnose and treat fungal infections, which are different from those of younger graduates[27]. Furthermore, it has been reported that dentists with more experience tend to see more patients in their practices[33], and this could be another explanation for the increased number of patients (more than three) diagnosed each month with oral candidiasis by our older graduates. Respondents with Jordanian qualifications used systemic antifungals significantly more often and diagnosed a greater number of cases of oral candidiasis. However, the country of qualification had no significant influence on the respondents' decision following diagnosis (referral *vs.* treatment). Supposedly, the specialty of oral medicine in Jordan has shown major improvements in terms of the number of practicing specialists and new oral medicine specialty programmes. These specialists are mainly affiliated with academic institutions and this has reflected favourably on the quality of teaching of oral medicine in Jordanian universities in recent years, as evident (in the present study) by the increased use of topical agents and some systemic antifungals by younger graduates.

In this study, respondents working in private practice diagnosed and referred a greater number of patients compared with those working in public practice. However, the use of fluconazole was their significant choice when treatment was intended. This could be linked to the findings related to professional practice, which was not considered in this survey because of the small number of specialists, particularly in oral medicine. These findings indicate that this small number of oral medicine specialists in Jordan is mainly affiliated to public institutions. Therefore, GDPs working in public practice are expected to encounter many patients who have already been diagnosed and referred from private practice. However, GDPs working in Jordanian public practice have limited options in prescribing, and this was evident in their significant prescribing of amphotericin, which is commonly available in hospital practices only. In the same way, fluconazole was not considered as one of the significant prescribing options for GDPs working in governmental institutions such as the Ministry of Health, Military Medical Services and university hospitals. This is in contrast to a recent study[27] that reported a non-significant association between the workplace of dentists and their attitude towards the treatment of oral candidiasis and their prescribing habits; however, the authors did not give an explanation for their findings.

Four antifungal drugs were preferred by participants in this study, namely (in descending order): nystatin, miconazole, amphotericin B and fluconazole. Nystatin was the most popular antifungal agent among the participants. It is also the drug most commonly prescribed by British dentists[21]; whereas, in Spain[27], miconazole was found to be slightly preferred to nystatin. Generally, topical agents, such as nystatin, clotrimazole and miconazole, are the preferred first line of antifungal therapy for most patients[30]. However, topical drug therapy is often unsuccessful for many reasons, such as the necessity of frequent daily dosing; rapid oral clearance of the drug, which leads to insufficient contact time with the oral mucosa; the need for adequate salivary flow; the presence of decay-inducing sweeteners; and inadequate efficacy[36]. The same applies to nystatin, which has a recommended dosage of four times a day for 2 weeks or more. The use of nystatin is characterised by a decrease of the drug concentration to a subtherapeutic level fairly quickly after administration as a result of the rapid oral clearance of the drug[37]. Furthermore, the risk of dental caries is increased because of its sucrose content[38]. Some novel approaches that have been proposed to increase the efficacy of nystatin include nanonsisation[39]. On the other hand, nystatin and amphotericin B (polyene antifungals) show negligible absorption from the gastrointestinal tract and are widely used for the topical treatment of oral candidiasis[37]. In addition, resistance to these agents has rarely been reported[40]. Lastly, it was reported that amphotericin B can be better tolerated than nystatin[41] and it is as effective as fluconazole for the treatment of

denture-induced stomatitis[42]. Miconazole is among the early antifungals first introduced in the late 1960s[37]. Having both antibacterial and antifungal activities, it is theoretically the best antifungal to treat angular cheilitis[37] and is an effective treatment for candida-associated denture stomatitis[43]. However, miconazole may potentiate the effect of warfarin[14], and it should be avoided in pregnancy and porphyria[37]. This interaction of miconazole with warfarin may appear more significant when using systemic preparations[21] of this and other antifungal agents, although, for oral lesions, miconazole is usually given in its topical form. On the other hand, a recent survey conducted by the AIDS Clinical Trials Group reported that clotrimazole, nystatin and fluconazole were the most popular antifungals prescribed for the treatment of oropharyngeal candidiasis[44].

This study found that amphotericin B was the third most commonly prescribed drug by respondents, followed by fluconazole and other less commonly available antifungal agents, such as ketoconazole and itraconazole. This is in agreement with studies in some European countries, such as Spain[27] and the UK[21], in which fluconazole was amongst the least commonly prescribed agents. Fluconazole was introduced in 1990[36], and it is generally safe and well tolerated[45]. However, it may be associated with an increased incidence of birth defects[46], proarrhythmic conditions[47] and hepatotoxicity[48]. Whereas azoles, in general, interact with anticoagulants, fluconazole is contraindicated in liver disease and is implicated in liver dysfunction[37]. Although it has been demonstrated that fluconazole is very effective for the treatment of oropharyngeal candidiasis, reports of resistance to this antifungal agent have been found[13]. Furthermore, certain non-*C. albicans* species, such as *Candida glabrata* and *Candida krusei*, show less susceptibility to fluconazole than other azole antifungals, and these are being recovered more frequently from patients with HIV[49]. Other antifungal agents, such as itraconazole and ketokonazole, were prescribed by a small proportion of respondents in this study and in a study conducted in Spain[27]. However, these agents were not available for dentists in the UK[21]. Fluconazole and itraconazole are better tolerated and more effective than ketoconazole[50]. Itraconazole has been reported to provide similar affectivity to fluconazole for the treatment of denture-induced stomatitis[51]. Indeed, among the oral azoles, fluconazole possesses the most desirable pharmacological properties, making it the drug of choice in the treatment of oro-pharyngeal candidiasis in HIV infection[37].

Chlorhexidine mouthwash was used by a substantial proportion of participants in the present study and by others[27]. However, chlorhexidine was cited by only 5% of UK dentists[21] as one of the treatment options other than the available conventional antifungal agents. The majority (93.2%) of our respondents who prescribed chlorhexidine, unlike dentists in the UK[21] and in Spain[27], reported its use as an adjunct to conventional antifungal agents, which indicates that they were selecting the appropriate drug therapies for fungal infections. Chlorhexidine belongs to the biguanide group and is active against a wide spectrum of microbial agents, including *C. albicans*. Therefore, it is widely prescribed by dentists to provide oral disinfection, particularly for denture wearers[52]. However, its adjunctive use with other antifungal agents is advocated[53], although its simultaneous use with nystatin would result in a drug–drug interaction[54]. Recently, some antimicrobial agents, such as cetylpyridinium chloride, have been incorporated in some mouthwashes to provide greater activity against fungal infections.[55].

Drug formulations preferred by our participants and by UK dentists[21] were nystatin pastilles and amphotericin B lozenges. However, drug formulations were not considered in a study conducted in Spain[27]. Nystatin pastilles have a number of favourable properties (e.g. they can be sucked slowly and they have a sweetened formulation), which lead to a longer duration of action and better patient compliance[37]. They could be used successfully in HIV-infected patients as a prophylaxis against outbreaks or recurrence of oral candidiasis[56]. Amphotericin B was chosen according to personal preference by a small percentage of our participants, although this drug is not always available in the Jordanian pharmaceutical market.

The findings of this survey do stress the need for new models of education for future health professionals education and clinical management of oral candidiasis in Jordan. Although it is difficult to predict the effect of any changes to the dental curricula and to provide clear national guidance on the pattern of prescribing and practice for the treatment of oral candidiasis among future dentists, the undergraduate and postgraduate curriculum should be enhanced with medical courses, such as oral microbiology and infectious diseases, delivered in a more comprehensive and productive way than at present. Other additional measures would include establishing oral medicine postgraduate training programmes to meet the requirements of the increasing numbers of patients with oral diseases. Furthermore, the JDA and other national health and academic agencies should provide clear guidance and training courses on the use of antifungals (amongst other antimicrobials) to all dental practitioners, regardless of their socio-professional background. In the light of the findings of this survey, there appears to be a significant influence of some socio-professional factors, such as experience, workplace and country of qualification, on the attitude of

respondents and their prescribing pattern. Implementing clear guidelines at a national level, such as those of the Expert Panel of the Infectious Diseases Society of America[16], for the management of patients with invasive and mucosal candidiasis, would be highly recommended to guide practitioners in achieving an accurate diagnosis and prescribing safe and effective treatment. Consequently, we hope that the drawbacks of antifungal prescribing in Jordan will be overcome. Such guidelines have to be generated, taking into consideration the standard requirements leading to effective and safe management of oral candidiasis, in terms of clinical type, the patient's medical condition, diagnostic skills, first- and second-line drugs, follow-up and documentation. This is again urgently needed in light of the data known on the importance of early detection of oral candidiasis, to prevent the development of invasive fungal infections and the associated high mortality rate[16]. Extra costs, as a result of prolonged hospital stay and greater use of hospital resources, will also be reduced. For instance, in the USA, a single hospital stay for the management of invasive candidiasis is estimated to be $40,000[16,57]. It is evident that Jordan now is in the middle of an unstable region politically with more immigrants coming from neighbouring countries and this generates more pressure on the health services, especially those provided by the Ministry of Health and armed forces hospitals, and primary care centres.

Despite the abovementioned results, this study is not without limitations. Differentiation between respondents prescribing antifungals simultaneously or those prescribing them according to the type of oral candidiasis, and between respondents prescribing antifungals as an initial first-line treatment or prescribing them after failure of the initial therapy, were not permitted by the design of the questionnaire. Similarly, the cost of patient care and the predisposing factors for oral candidiasis, such as denture wearing or some underlying systemic conditions, were not investigated. The exclusion of 93 completed questionnaires, the small sample size and the method of sample selection were additional limitations; it was a cross-sectional questionnaire-based survey and only dentists who were present in the practitioners' list obtained from the JDA were selected. Therefore, future studies will have to incorporate a larger sample to provide findings that are nationally representative and able to confirm the results of this survey.

CONCLUSION

The attitude towards the treatment of oral candidiasis is more positive among the least-experienced GDPs who are working in private practice. Nystatin and miconazole are the most popular choices of antifungal agents among Jordanian dentists who showed proper treatment of oral candidiasis and adequate selection of recommended topical and systemic antifungal agents and formulations. Topical treatment is most commonly used among male GDPs and younger graduates, whereas systemic treatment is commonly used among dentists who graduated from Jordan.

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CONTRIBUTION

Mohammad H. Al-Shayyab: correspondence, idea, hypothesis, study design, acquisition of data, statistical analysis, interpretation of data, writing the article, revising it critically for important intellectual content and final approval of the version to be submitted and published. *Osama A. Abu-Hammad and Najla S. Dar-Odeh*: idea, hypothesis, substantial contributions to conception and design of and acquisition of data, revising it critically for important intellectual content and final approval of the version to be submitted. *Mahmoud K. AL-Omiri*: substantial contributions to conception and design of and acquisition of data, consulted on statistical evaluation, revising it critically for important intellectual content.

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