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HEALTHCARE WORKERS PERCEPTIONS REGARDING ANTIBIOTIC USE DURING COVID-19 PANDEMIC IN LEBANON: A CROSS-SECTIONAL STUDY

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HEALTHCARE WORKERS PERCEPTIONS REGARDING ANTIBIOTIC USE DURING COVID-19 PANDEMIC IN LEBANON: A CROSS-SECTIONAL STUDY

Abstract

Since the beginning of the COVID-19 pandemic, empirical antibiotics prescription has increased globally in patients with COVID-19 for suspected or confirmed bacterial infection. Hence, concerns have been raised about potential rise in antibiotic resistance that will create further challenges for antimicrobial stewardship. This descriptive cross-sectional study was conducted to assess healthcare workers attitudes and practices regarding antibiotics prescription during the COVID-19 pandemic in Lebanon. The survey was distributed online using GOOGLE forms and included questions addressing socio-demographic characteristics, trainings in antibiotics use and healthcare workers attitudes and practices regarding antibiotics prescription during the pandemic. In total, 399 healthcare workers responded to the survey. Less than half of them had already participated in antibiotic prescription trainings before or during the pandemic. However, only 11% participated, mostly nurses, in antibiotic stewardship program. Azithromycin was the most prescribed antibiotic with Vitamin C and Zinc used as second line treatments in COVID-19 patients. In addition, nearly two-third of the participants reported an increase in antibiotic use during the early phase of the pandemic and considered that COVID-19 patients are receiving unnecessary antibiotics. This study showed excessive antibiotics prescription during the COVID-19 pandemic in Lebanon that needs to be tackled by raising awareness of antimicrobial stewardship and control measures.

Keywords

COVID-19 pandemic, Antibiotic use, Attitudes, Practices, Health care workers

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by the new coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which first appeared in Wuhan, China in December 2019 (WHO, 2020). In Lebanon, the first case of coronavirus was confirmed on February 21, 2020. Henceforth, Lebanon has had over 400,000 cases with worldwide cases reaching over 120 million confirmed cases across 221 countries and territories and over 2 million deaths. COVID-19 is characterized by typical symptoms including fever, dry cough and fatigue and other less common symptoms such as losing smell or taste, muscle pain, nasal congestion and nausea or vomiting (WHO, 2020). Around 80% of COVID-19 infected patients do not require hospitalization, 15% can become severely ill and only 5% become critically ill requiring hospitalization (WHO, 2020). Strikingly, the pandemic has been followed by an increased use and prescription of antibiotics which will hasten antimicrobial resistance (AMR) development (Beović et al., 2020).

COVID-19 has shifted the focus of healthcare workers and created further challenges to the health and social care systems with huge strains being placed on global resources (Rawson et al., 2020a). Critically ill COVID-19 patients are susceptible to develop secondary infections, however, the empiric use of antibiotics can lead to an increase in AMR (Seaton et al., 2020). AMR is perceived as a real global challenge threatening human and animal health. Several associations, international agencies, and governments have emphasized the urgency of this problem (Rodríguez-Álvarez et al., 2020). The pattern of AMR will unquestionably change with the emergence of COVID-19 pandemic. Therefore, it is critical to consider and evaluate the outcomes of this pandemic on the use of antibiotics and AMR (Rawson et al., 2020b). In addition, it is essential to develop antimicrobial policies and guidelines by auditing the prescription of antibiotics and implementing AMR surveillance systems and monitoring (Rawson et al., 2020b).

According to the World Health Organization (WHO), antibiotic therapy or prophylaxis should not be used in patients with mild or moderate COVID-19 unless it is indicated (WHO, 2020). The use of antibiotics should be reserved for suspected or confirmed bacterial or fungal respiratory co-infections in patients with COVID-19 (Rawson et al., 2020a). Studies showed that bacterial co-infection might lead to increased morbidity and mortality in COVID-19 patients (Liu et al., 2021). Therefore, it was expected that these patients will receive empirical antibiotic therapy (Rawson et al., 2020a), however, most patients received the therapy before even being diagnosed with bacterial infection (Liu et al., 2021). Moreover, recent studies showed that the rate of bacterial co-infection in COVID-19 patients is low. Nevertheless, overprescribing of antibiotics is evident and use of broad-spectrum antibiotics is high (Rawson et al., 2020b). For this reason, healthcare systems must manage the optimal selection of empirical therapy. This should be followed by the de-escalation of antibiotics when appropriate by enforcing antibiotic stewardship programs (ASPs) (Rawson et al., 2020a). However, the basis for the empirical prescription of antibiotics in suspected COVID-19 patients is not well identified (Seaton et al., 2020).

Implementation of effective policies and guidelines is crucial to evaluate the antimicrobial use in COVID-19 patients and hence to mitigate the unintended consequences of the redundant use of antibiotics and its impact on AMR (Rawson et al., 2020a; Stevens et al., 2021). Moreover, healthcare systems must ensure that healthcare workers receive training and education in safe and judicious antimicrobial prescribing, in addition to ASPs for the management and the optimal use of antibiotics (Rawson et al., 2020a). Educating physicians about safe antibiotic practices could reduce antibiotic prescribing. However, this education must extend to other health care workers including nurses, the first healthcare workers to come into contact with COVID-19 infected patients, and pharmacists who assist in managing this public health issue by acting as a source of vital information to patients about COVID-19 (Bukhari et al., 2020). The combined efforts of healthcare workers and their participation is vital to end this outbreak. Therefore, focus on providing sufficient knowledge to physicians, nurses, and pharmacists regarding antibiotic use is essential especially during the COVID-19 pandemic in order to diminish the collateral consequences of this pandemic on the issue of AMR. However, there is limited data regarding knowledge and attitudes of healthcare workers regarding antibiotic use in COVID-19 patients. To the best of our knowledge, such a study has not been conducted in Lebanon till now. Therefore, the purpose of this study is to assess the perception of healthcare workers regarding antibiotic use during the COVID-19 pandemic in Lebanon.

2. METHODOLOGY

2.1 Study Design and Population

This cross-sectional study was conducted amongst physicians, nurses and pharmacists in Lebanon. The population size was estimated at 31.000 based on data obtained from the Lebanese order of physicians (LOP), the Order of Nurses in Lebanon (ONS) and the Order of Pharmacists of Lebanon (OPL). The calculated sample size was found to be minimum of 385 for a desired 95% confidence interval with 5% margin of error. Considering a drop out level of 10%, the final minimum sample size is estimated at 428. Only 400 healthcare workers participated in the study with only one participant was excluded from the study due to missing information. Participants were selected through convenience sampling. Healthcare workers needed to meet the following inclusion criteria: being a physician, nurse or pharmacist currently practicing in Lebanon for more than one year. No exclusion criteria were used.

2.2 Study Survey

The survey was adopted from previous studies (Seaton et al., 2020; Liu et al., 2021) and adjusted to meet the study objectives. Questions were divided into 3 categories: socio-demographics, trainings in antibiotics use and healthcare workers attitudes and practices regarding antibiotics prescription during the COVID-19 pandemic. The survey was distributed online using GOOGLE forms through Emails and phones (WhatsApp). A pilot study was conducted to test the integrity and comprehension of the questions.

2.3 Ethical Consideration

This study followed the guidelines of the Declaration of Helsinki on the conduct of human research and was approved by the Institutional Review Board of the university under the number (2021-H-0120-HS-R-0439e22). Two reminders were sent to each participant and all participants consent online to participate in this study. All data collected were anonymous and questionnaires were gathered and checked for completeness by the principal investigator.

2.4 Statistical Analysis

Statistical Package of Social Science (IBM SPSS, version 23) was used for data entry, cleaning, management, and analyses. Descriptive analyses were carried out by calculating the mean and standard deviation for continuous variables, and number and percentages for categorical variables. Inferential statistics, mainly bivariate analyses were carried out by using the Chi-square test for categorical variables. A p-value <0.05 was considered significant.

3. RESULTS

3.1 Socio-demographic information of participants

399 healthcare workers participated in the study almost equally distributed between female and male. 60.2% were physicians among whom 40.2% were specialized in internal medicine. Most of the participants worked in private clinics, hospitals or pharmacies. 64% took care of COVID-19 patients and 57.1% treated COVID-19 patients (**Table I**).

Table I: Socio-demographic information of participants. S.D is the standard deviation.

Year of Experience	Mean ± S.D	
	12.79 ± 10.76	
	Number	Percentage
Gender (399)		
Female	190	47.6
Male	209	52.4
Occupation (398)		
Nurse	64	16.1
Pharmacist	94	23.6
Physician	240	60.2
Physicians' specialty (229)		

Family medicine	25	10.9
Pediatric	30	13.1
Internal medicine	92	40.2
Surgery/Anesthesia	49	21.4
Obstetrics/Gynecology	20	8.7
Others	13	5.7
Place of work (399)		
Private	320	80.2
Public	23	5.8
Both	56	14.0
Care of patients with COVID-19 (399)		
Yes	258	64.7
No	141	35.3
Treatment of patients with COVID-19 (399)		
Yes	228	57.1
No	171	42.9

3.2 Participants' involvement in antibiotics prescription trainings and their perception regarding the use of antibiotic during the COVID-19 pandemic

48.9% of healthcare workers had already participated in antibiotic prescription trainings before the COVID-19 pandemic, and only 39.3% participated in similar activity during the pandemic. Two third of participants had received seminars and lectures regarding antibiotic prescription. However, only 11% participated in antibiotic stewardship program during COVID-19 (Table II).

Table II: Participants' involvement in antibiotic prescription trainings and their perception regarding antibiotic use during the COVID-19 pandemic.

	Number (n)	Percentage (%)
Training in antibiotic prescription before the COVID-19 pandemic (399)	195	48.9
Yes	204	51.1
No		
Training in antibiotic prescription during the COVID-19 pandemic (399)	157	39.3
Yes	242	60.7
No		
Source of training (157)		
Seminars/ Lectures	104	66.2
Web-based education	53	33.8
Training in Antibiotic Stewardship Program during the COVID-19 pandemic (399)		
Yes	44	11
No	355	89
Antibiotics use during the early phase of the COVID-19 pandemic (399)	263	65.9
Increase	93	23.3
Same	43	10.8
Decrease		
Change in antibiotic use after COVID-19 understanding (399)		
Yes	196	49.1
No	113	28.3
I don't know	90	22.6
Patients requested more antibiotics (399)		
Yes	264	66.2
No	77	19.3
I don't know	58	14.5
COVID-19 patients are receiving unnecessary antibiotics (399)		
Yes	284	71.2
No	65	16.3
I don't know	50	12.5
Inappropriate use of antibiotics in COVID-19 patients (399)		
Significant	303	75.9
Insignificant	96	24.1
Antibiotics use increases mortality in COVID-19 patients (399)		

Yes	57	14.3
No	213	53.4
I don't know	129	32.3
Prescription of antibiotics will change with the emergence of a new strain (399)		
Yes	132	33.1
No	155	38.8
I don't know	112	28.1
Emergence of a new strain (399)		
Increase	115	76.2
Decrease	36	23.8
Drug resistance situation (399)		
Yes	318	79.7
No	32	8.0
I don't know	49	12.3
Magnitude of emerging antibiotic resistance as a healthcare problem (399)		
Not Urgent	141	35.3
Urgent	258	64.7

Regarding participants' perception towards antibiotic use during the COVID-19 pandemic, 65.9% witnessed an increase in antibiotic use during the early phase of the pandemic and almost half thought that antibiotic use has changed after the understanding of COVID-19 (**Table II**).

During the COVID-19 pandemic, 71.2% of healthcare workers considered that COVID-19 patients are receiving unnecessary antibiotics, 75.9% rated significantly inappropriate use of antibiotics, 33.1% stated that antibiotics prescription will change with the emergence of a new strain, 79.7% believed that prescription behavior influences the drug resistance situation in the area, and 64.7% perceived the magnitude of emerging antibiotic resistance as an urgent healthcare problem. However, only 14.3% found that antibiotic use increases mortality in COVID-19 patients (**Table II**).

3.3 Nurses and physicians' practices regarding antibiotic use among COVID-19 patients

66.8% of the healthcare workers followed guidelines for the antibiotic use among COVID-19 patients, 44.8% witnessed restrictions on the use of antibiotics and 48.4% used conducted examination on the need of antibiotics. In addition, 48.7% of them performed antibiotic revisions based on cultures, 57.8% discontinued antibiotics administration when needed based on symptoms relief, and 46.3% used narrow spectrum antibiotics when fever was the common medical sign. However, only 19% of the participants performed daily electronic audit (**Table III**).

Table III: Nurses and physicians practices in antibiotic use among COVID-19 patients. Number of respondents is 304 unless indicated.

	Number (n)	Percentage (%)
Restriction on the use of antibiotics		
Yes	136	44.7
No	100	32.9
I don't know	68	22.4
Thorough examination		
Yes	147	48.4
No	82	27
I don't know	75	24.6
Daily electronic audit		
Yes	58	19.1
No	198	65.1
I don't know	48	15.8
Antibiotic revision		
Yes	148	48.7
No	106	34.9
I don't know	50	16.4

	Number (n)	Percentage (%)
Antibiotic discontinuation		
Yes	176	57.9
No	69	22.7
I don't know	59	19.4
Antibiotic discontinuation based on (295)		
Laboratory tests	43	14.6
Symptoms	136	46.1
Both	116	39.3
Type of empirical use of antibiotics (301)		
Narrow spectrum	138	45.8
Broad spectrum	42	14
Both	121	40.2
Following specific guidelines		
Yes	203	66.8
No	50	16.4
I don't Know	51	16.8
Symptoms for empirical prescription of antibiotics		
Fever	202	77.7
Expectoration	151	57.9
Cough	140	53.6
Expiratory dyspnea	96	36.8
Chest tightness	71	27.2
Weakness	34	13
COVID-19 status for empirical prescription of antibiotics		
Positive test	140	53
Suspected on admission	83	31.5
Probable or definite nosocomial COVID-19	136	51.5

3.4 Healthcare workers' perceptions of antibiotics use during the COVID-19 pandemic and trainings in antibiotics prescription

The most used antibiotics were Azithromycin (87.7%), Ceftriaxone (34.6%), Piperacillin/Tazobactam (25.4%) and Moxifloxacin (18.2%) and the least prescribed were Gentamycin (1%) and Metronidazole (3.4%). The main route of administration was orally (87%) followed by intravenously (63.2%). The course of antibiotics administration was between 5 to 7 days (55%). Vitamin C (91.5%) and Zinc (89.1%) were widely used as second line treatments in COVID-19 patients (Table IV).

Table IV: Antibiotics and other medications regimen used by healthcare workers among COVID-19 patients.

	Number (n)	Percentage (%)
Antibiotic		
Azithromycin (367)	322	87.7
Ceftriaxone (318)	110	34.6
Piperacillin/Tazobactam (307)	78	25.4
Moxifloxacin (302)	55	18.2
Doxycyline (299)	49	16.4
Ciprofloxacin (297)	42	14.1
Vancomycin (294)	30	10.2
Levofloxacin (253)	25	9.8
Cefepime (294)	39	8.5
Clindamycin (292)	14	4.8
Ampicillin (292)	13	4.5
Amoxycillin (293)	21	7.2
Metronidazole (291)	10	3.4
Gentamycin (289)	3	1
Route of administration		
Oral (368)	320	87
Intravenous (329)	208	63.2
Intramuscular (292)	13	4.5
Course of antibiotic administration (378)		
Less than 5 days	36	9.5
5-7 days	209	55.3
8-10 days	83	22.0

10-14 days	50	13.2
Other first-line treatments		
Vitamin C (375)	343	91.5
Zinc (377)	336	89.1
Antiviral therapy (329)	136	41.3
Vitamin D (386)	52	13.4

A significant association was identified between healthcare workers occupation and stewardship training, perception of antibiotic use during the early phase of the pandemic, antibiotics request by patients and the effect of antibiotic prescription on the emergence of new strains (**Table V**). Stewardship training was significantly more observed among nurses (23.4%) than physicians (8.3%). Moreover, pharmacists (51.1%) believed significantly, more than physicians (27.5%), that the use of antibiotics will affect the emergence of new strains. Healthcare occupation did not affect the other perceptions (**Table V**).

Table V: Differences in healthcare workers' practices regarding antibiotic use during the COVID-19 pandemic. * represents the variables that showed a significant association.

	Number (Percentage)			p value
	Nurse	Physician	Pharmacist	
Training in antibiotic prescription before the COVID-19 pandemic				0.38
Yes	30 (46.9)	124 (51.7)	41 (43.6)	
No	34 (53)	116 (48.3)	53 (56.4)	
Training in antibiotic prescription during the COVID-19 pandemic				0.2
Yes	23 (35.9)	103 (42.9)	31 (33)	
No	61 (64.1)	137 (57.1)	63 (67)	
Training in antibiotic stewardship program during the COVID-19 pandemic				0.002
Yes	15 (23.4) *	20 (8.3) *	9 (9.6)	
No	49 (76.6)	220 (91.7)	85 (90.4)	
Antibiotic use during the early phase of the COVID-19 pandemic				0.015
Increase	32 (50) *	158 (65.8)	72 (76.6) *	
Same	23 (35.9)	55 (22.9)	15 (16)	
Decrease	9 (14.1)	27 (11.3)	7 (7.4)	
Change in antibiotic use after COVID-19 understanding				0.065
Yes	30 (46.9)	114 (47.5)	52 (55.3)	
No	13 (20.3)	70 (29.2)	29 (30.9)	
I don't know	21 (32.8)	56 (23.3)	13 (13.8)	
Patients requested more antibiotics				0.000
Yes	40 (62.5)	162 (67.5)	61 (64.9)	
No	6 (9.4)	57 (23.8)	14 (14.9)	
I don't know	18 (28.1) *	21 (8.8) *	19 (20.2)	
COVID-19 patients are receiving unnecessary antibiotics				0.36
Yes	39 (60.9)	174 (72.5)	70 (74.5)	
No	13 (20.3)	38 (15.8)	14 (14.9)	
I don't know	12 (18.8)	28 (11.7)	10 (10.6)	
Inappropriate use of antibiotics in COVID-19 patients				0.42
Significant	45 (70.3)	187 (77.9)	70 (74.5)	
Insignificant	19 (29.7)	53 (22.1)	24 (25.5)	
Antibiotic use increases mortality in COVID-19 patients				0.07
Yes	10 (15.6)	27 (11.3)	20 (21.3)	
No	39 (60.9)	129 (53.8)	44 (46.8)	
I don't know	15 (23.4)	84 (35)	30 (31.9)	

Prescription of antibiotics will change with the emergence of a new strain				0.01
Yes	17 (26.6)	66 (27.5) *	48 (51.1)*	
No	25 (39.1)	104 (43.3)	26 (27.7)	
I don't know	22 (34.4)	70 (29.2)	20 (21.3)	
Drug resistance situation				0.057
Yes	43 (67.2)	195 (81.3)	79 (84)	
No	7 (10.9)	17 (7.1)	8 (8.5)	
I don't know	14 (21.8)	28 (11.7)	7 (7.4)	
Magnitude of emerging antibiotic resistance as a healthcare problem				0.76
Not Urgent	21 (32.8)	84 (35)	36 (38.3)	
Urgent	43 (67.2)	156 (65)	58 (61.7)	

When determining the effect of antibiotics training on healthcare workers perception regarding antibiotic use, an increase in healthcare workers knowledge regarding the unnecessary use of antibiotics and influence on drug resistance was observed. Additionally, data in this study revealed a significant association with healthcare belief that antibiotic prescription would increase mortality (**Table VI**).

Table VI: Association between antibiotic prescription training and perception of antibiotic use during the COVID-19 pandemic. * represents the variables that showed a significant association.

	Number (Percentage)		p value
	Yes	No	
Training in antibiotic prescription			
COVID-19 patients are receiving unnecessary antibiotics			0.004
Yes	122 (77.7)	162 (66.9)	
No	26 (16.6)	39 (16.1)	
I don't know	9 (5.7) *	41 (16.9) *	
Inappropriate use of antibiotics in COVID-19 patients			0.72
Significant	121 (77.1)	182 (75.2)	
Insignificant	36 (22.9)	60 (24.8)	
Antibiotic use increases mortality in COVID-19 patients			0.001
Yes	32 (20.4)*	25 (10.3) *	
No	88 (56.1)	125 (51.7)	
I don't know	37 (23.6)	92 (38)	
Prescription of antibiotics will change with the emergence of a new strain			0.12
Yes	61 (38.9)	71 (29.3)	
No	58 (36.9)	97 (40.1)	
I don't know	38 (24.2)	74 (30.6)	
Drug resistance situation			0.01
Yes	129 (82.2)	189 (78.1)	
No	17 (10.8)	15 (6.2)	
I don't know	11 (7) *	38 (15.7) *	
Magnitude of emerging antibiotic resistance as a healthcare problem			0.07
Not Urgent	64 (40.8)	77 (31.8)	
Urgent	93 (59.2)	165 (68.2)	

3.5 Impact of ASP on nurses and physicians' perception regarding antibiotic use among COVID-19 patients

ASP training during the COVID-19 pandemic among nurses and physicians was significantly associated with the following practices: training in antibiotic use before and after the COVID-19 pandemic, restriction on the use of antibiotics, examination conducted on the need of antibiotics, daily electronic audit, antibiotic revision and following guidelines regarding the use of antibiotics in COVID-19 patients. All these practices were significantly enhanced among nurses and physicians that had participated in ASP (**Tables VII**).

Table VII: Association between stewardship training and antibiotic prescription practice among nurses and physicians.

Stewardship training	Number (Percentage)		p value
	Yes	No	
Training in antibiotic prescription before the COVID-19 pandemic			0.000
Yes	29 (82.9)	125 (46.1)	
No	6 (17.1)	146 (53.9)	
Training in antibiotic prescription during the COVID-19 pandemic			0.000
Yes	28 (80)	98 (36.2)	
No	7 (20)	173 (63.8)	
Restriction on the use of antibiotics			0.008
Yes	24 (68.6)	113 (41.7)	
No	8 (22.9)	93 (34.3)	
I don't know	3 (8.6)	65 (24)	
Thorough examination			0.004
Yes	26 (74.3)	122 (45)	
No	6 (17.1)	76 (28)	
I don't know	3 (8.6)	73 (26.9)	
Daily electronic audit			0.000
Yes	19 (54.3)	39 (14.4)	
No	13 (37.1)	186 (68.6)	
I don't know	3 (8.6)	46 (17)	
Antibiotic revision			0.000
Yes	28 (80)	121 (44.6)	
No	3 (8.6)	103 (38)	
I don't know	4 (11.4)	47 (17.3)	
Antibiotic discontinuation			0.21
Yes	18 (51.4)	159 (58.7)	
No	12 (34.3)	58 (21.4)	
I don't know	5 (14.3)	54 (19.9)	
Following specific guidelines			0.034
Yes	30 (85.7)	173 (63.8)	
No	2 (5.7)	50 (18.5)	
I don't Know	3 (8.6)	48 (17.7)	

4. DISCUSSION

The COVID-19 pandemic is currently a major health threat exhibiting a chaotic and profound impact on all aspects of health care including the steady increase in antimicrobial resistance. It is worth mentioning that the irrational use of antibiotics in COVID-19 patients will exacerbate the concern of AMR beyond the COVID-19 pandemic, thus the establishment of an antibiotic stewardship program is crucial to tackle this issue while promoting the optimization of antibiotic therapy. Currently, studies conducted among healthcare providers on antibiotic use during the COVID-19 pandemic are scarce. In this regard, we conducted this study to assess knowledge, attitudes, and practices regarding prescribing patterns of antibiotics during the COVID-19 pandemic among Lebanese healthcare providers.

Presently, there are no drugs or therapeutics approved for COVID-19 disease. Recent clinical evidence has emphasized the supportive role of nutritional supplementation in COVID-19 patients. In our study, the most common supplements prescribed as immune system boosters were Vitamin C (91.5%) and Zinc (89.1%). Vitamin C has antimicrobial and immunomodulatory properties and works as scavenger of reactive oxygen species (Mousavi et al., 2019; Mešćić Macan

et al., 2019). It can counteract the cytokine storm that diminishes the host immune response exacerbating the acute respiratory distress syndrome (ARDS) (Härtel et al., 2004; Jovic et al., 2020; Feyaerts & Luyten, 2020). The prescription of both Vitamin C and Zinc in addition to other mineral supplementation or “immunonutrition” (Vitamins A, B, D and E) is crucial to mitigate the COVID-19 devastating effects (Jovic et al., 2020).

Regarding the antibiotic therapy during the COVID-19 pandemic, the findings of this study showed an increase in antibiotic use during this period. In addition, the participants reported the administration of oral antibiotics as empiric therapy in patients with probable or definite nosocomial COVID-19 (51.5%), or patients who tested positive for COVID-19 (53%). Fever was the most common symptom (77.7%) that guides the prescription of empiric antibiotic regimen to non-hospitalized and hospitalized patients. The increase of antibiotic use in this study is consistent with a multi-hospital cohort study, conducted in Michigan, which showed an increase in the prescription of early empiric antibacterial therapy (56.6% of the hospitalized COVID-19 patients), whilst only 3.5% were diagnosed with bacterial infection (Vaughn et al., 2021). Similar findings were reported in other studies emphasizing on the early empiric antibiotics prescription in patients hospitalized with COVID-19 (Rawson et al., 2020a; Guan et al., 2020; Langford et al., 2020; Lansbury et al., 2020).

Although two-thirds of the healthcare providers that participated in our study declared that they follow specific guidelines in antibiotic administration, data showed that the prescription was not evidence-based and designed without prior culture-proven identification of bacterial pneumonia to differentiate it from COVID-19 pneumonia. The widespread of antibiotic use in Lebanon and other countries may stem from the clinicians experience that treated patients who had bacterial coinfections during influenza pandemic (Nestler et al., 2021).

Moreover, the participants reported that azithromycin was the first most commonly prescribed antibiotic to treat COVID-19 patients, followed by ceftriaxone. The widespread prescription of azithromycin, worldwide, was reported mostly during the early phase of the pandemic; however, the evaluation of the practice patterns of the surveyed Lebanese healthcare providers revealed continued prescribing of this antibiotic. Azithromycin is a semisynthetic macrolide with a broad-spectrum bacteriostatic activity against Gram-positive bacteria and some community-acquired Gram-negative pathogens. Beyond their antimicrobial properties, the effectiveness of macrolides use in respiratory viral infections is controversial. Macrolide antibiotics are reported for their anti-inflammatory and immunomodulatory effects, they mitigate the production of pro-inflammatory cytokines and attenuate virus-induced exacerbations (Min & Jang, 2012). These striking features render them promising drug candidates for treating the cytokine storm which is a prominent hallmark of severe influenza A and COVID-19 diseases. Our findings are consistent with other studies that showed increased use of broad-spectrum antibiotics including azithromycin and ceftriaxone during the early phase of the pandemic (Nestler et al., 2021; Abelenda-Alonso et al., 2020). Additionally, a recent Canadian meta-analysis revealed similar antibiotic prescribing practices to nearly three-quarters of patients with COVID-19, whereas the prevalence of bacterial co-infections was 8.6% (Langford et al., 2020). Recent studies reported a clinical efficacy of the hydroxychloroquine and azithromycin combined treatment for virus elimination in addition to a decrease in mortality in patients with severe COVID-19 (Arshad et al., 2020; Gautret et al., 2020). Furthermore, a retrospective observational study conducted in an American tertiary-care academic medical center reported that approximately two-thirds of COVID-19–confirmed patients received an antibiotic. It also demonstrated an increase in both azithromycin and ceftriaxone use for COVID-19 patient care teams compared to pre–COVID-19 levels, but followed by significant antimicrobial use reduction, resulting from the implementation of clinical guidance team who recommended the cessation of azithromycin use for COVID-19 treatment alone, and the discontinuation of antibiotic therapy in patients with confirmed COVID-19. However, ceftriaxone use in that study did not show any significant change (Staub et al., 2021). Despite the fact that they improve the clinical outcomes of hospitalized patients with severe COVID-19, there is no significant evidence on the efficacy of including macrolides to the treatment regimen for COVID-19 patients. A randomized clinical trial, conducted in Brazil, showed that the use of azithromycin in a combination therapy with hydroxychloroquine has no effect on the clinical outcomes of patients with severe COVID-19 (Furtado et al., 2020). Another observation study conducted in a French teaching hospital reported a significant reduction in the prescription of the combination of hydroxychloroquine with azithromycin from the beginning of

April 2020 (Gourieux et al., 2021). Notably, studies showed that prevalence of bacterial coinfection is very low (<5%) and antibiotics should not be routinely used unless a bacterial coinfection is suspected. Consequently, the WHO and Chinese guidelines discouraged inappropriate and routine empirical antibiotic treatment, especially the broad-spectrum antibacterial drugs, in patients without suspected or confirmed severe COVID-19 (WHO, 2020; Zhang et al., 2020).

In this study, more than two thirds of the participants agreed that unneeded and over-prescribed antibiotics across health care settings will contribute to antimicrobial resistance; and described the emergence of antibiotic resistance as an urgent healthcare issue. In response to the pandemic, healthcare settings have rapidly implemented prophylactic antibiotic regimen in the first-line treatment for COVID-19. This adaptation may be explained by disease severity on admission despite few reports of bacterial coinfection. Furthermore, most of the surveyed nurses and physicians in our study reported that they don't perform daily electronic audit, and nearly half of them don't conduct a thorough examination regarding whether a patient is in need of antibiotics and don't incorporate formulary restrictions into the drug ordering process. In addition, they don't perform culture-based revisions but the discontinuation of antibiotics therapy is based on symptoms relief. All these findings could be explained by the limited training and education provided on antibiotic stewardship program, since only 11% of the healthcare providers had participated in this program. In this regard, antibiotic stewardship training program during the COVID-19 pandemic among nurses and physicians was significantly associated with training, restrictions on antibiotic use, adherence to practice guidelines, and other patterns related to monitoring of antimicrobial use. These practices were significantly improved among nurses that had participated in ASP. Hence, excessive antibiotics prescription may be explained by lack of attention to the implementation and support of stewardship in healthcare settings that could improve the rational and judicious use of antibiotics. Engagement and education of healthcare providers is crucial to mitigate inappropriate use of antibiotics during the COVID-19 pandemic, and thus antimicrobial resistance (Liew et al., 2020).

The present study is the first nationwide descriptive analysis that reveals the current situation and reflects the antibiotic prescribing practices among Lebanese healthcare providers during the COVID-19 pandemic. However, the interpretation of our findings must be considered in the context of limitations. First, the cross-sectional design of the survey demonstrated associations with no evidence of temporal relationships. Second, we did not have data on secondary bacterial infections that could further explain the use of antibiotics. Third, proportional allocation of healthcare practitioners was not reached during data collection.

5. CONCLUSION

The present study evaluated the perception of healthcare workers regarding antibiotic use during the COVID-19 pandemic in Lebanon. The findings showed that less than half of the participants had already participated in antibiotic prescription trainings. However, the participation in antibiotic stewardship program was limited. In addition, nearly two-third of the participants reported an increase in antibiotic use, especially Azithromycin, during the early phase of the COVID-19 pandemic. This study highlights the urgent need to implement antimicrobial stewardship programs in health systems to halt the spread of antibiotic resistance and effectively handle any future pandemics and health risks in the country.

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