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Coronavirus Pandemic

The potential counter effect of COVID-19 outbreak on an antimicrobial agents prescribing educational intervention

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Abstract

Introduction: Educational interventions targeting health care professionals can contribute to improving knowledge and behaviors of antimicrobial agents prescribing. However, the unprecedented COVID-19 outbreak caused a disruption of the current practices and treatment guidelines. Therefore, it is highly likely that the pandemic had its disruptive effect on any educational interventions that were going on during the outbreak. This study aims to evaluate the effectiveness of an educational intervention in improving antimicrobial agents prescribing

Methodology: This was a randomized controlled study that included 69 resident physicians in a teaching hospital. The intervention group received an educational intervention focusing on antimicrobial agents prescribing and resistance. Before and after the intervention, outpatient antimicrobial agents prescribing rates for the two study arms were compared for the pre- and post-intervention periods. Additionally, all participants were asked to complete an online questionnaire that measured their knowledge, attitudes and behavioral intention towards antimicrobial agents resistance and prescription. The post-intervention period included the months of February, March, and June 2020. April and May were excluded from the study period since clinics were closed due to the COVID -19 pandemic.

Results: Post-intervention, the rate of antimicrobial agents prescribing by the intervention group was significantly higher than that of the control group ($p < 0.001$). Mean fear score for the intervention group was significantly lower than that for the control group after the intervention.

Conclusions: Findings indicate failure of the educational intervention in improving antimicrobial agents prescribing. However, an unexpected counter effect of the COVID-19 outbreak is highly likely.

Key words: Antimicrobial agents; COVID-19; education.

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Introduction

The discovery of antimicrobial agents played a significant role in treating bacterial infections previously deemed life-threatening [1]. However, several bacterial infections including lower respiratory tract infections are still listed among the most common causes of death according to the World Health Organization (WHO) [2]. Such predicament could be mainly attributed to the antimicrobial resistance crisis, which threatens a transition to an era where antimicrobial agents are no longer effective [1]. Antimicrobial resistance is a growing global challenge to public health, especially with the rapid development of multi-drug resistant bacterial strains in recent years. As a result, antimicrobial resistance places a continuous demand on the production of antibacterial drugs, which in turn increases the burden on governments and pharmaceutical companies [3].

One of the major factors playing a role in developing antimicrobial resistance is inappropriate prescribing behavior [4]. This can be manifested in several aspects including uncertainty of diagnosis, patients' persistence on receiving antimicrobial agents, inadequate prescribing guidelines, avoidance of possible complications arising in patients, and ignorance of prescribing behavior as being a cause of antimicrobial agents resistance [5,6]. For instance, longer treatment courses of antimicrobial agents courses and overprescribing were associated with higher rates of resistance, especially when treating self-limiting upper respiratory tract infections with antimicrobial agents [7]. Evidence suggests that inadequate testing facilities, time constraints, and insufficient guidelines added significant challenge to proper prescribing of antimicrobial agents [8]. Moreover, it has been found that patients influence physicians' prescribing behavior through increased pressure and possibility of changing physicians if no antimicrobial agents prescription was provided [5,9].

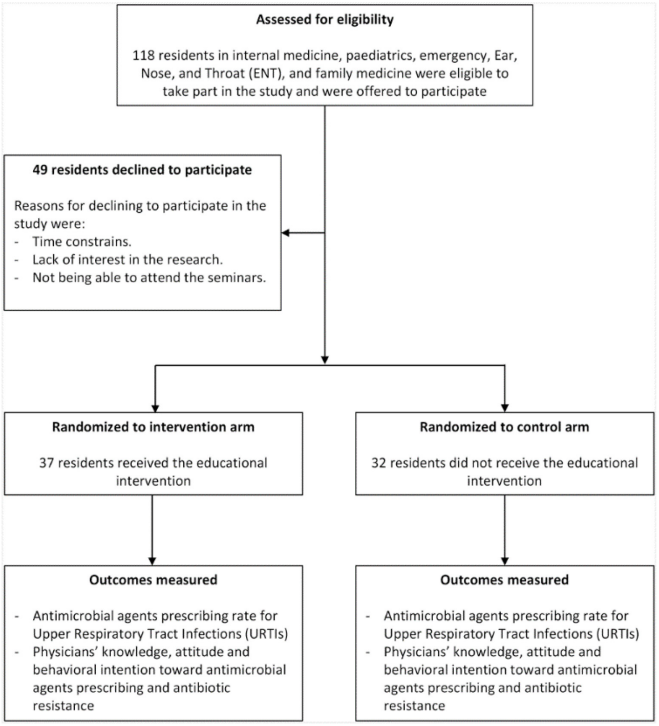
In Jordan, antimicrobial resistance is a rising problem that imposed a potential burden to the country's healthcare system [10,11]. Such increase in antimicrobial resistance can be explained by several factors including unnecessary antimicrobial agents prescribing at health clinics, high accessibility to antimicrobial agents due to dispensing of non-prescription and prescription antimicrobial agents by pharmacists, overt dispensing of prescription antimicrobial agents, or assumption on the physicians' behalf that antimicrobial agents would provide prophylaxis for patients [12-15].

This randomized controlled trial was designed to assess the effectiveness of an educational intervention in improving the antimicrobial agents prescribing behavior of residents at Jordan University Hospital in Amman, Jordan. The study also assessed the impact of the educational intervention on residents' knowledge, attitude, and behavioral intention towards antimicrobial resistance. However, the COVID-19 outbreak is thought to be an unexpected confounding factor that might have had a counter effect on the efficacy of the suggested educational intervention.

Methodology

This study is a randomized controlled trial that aimed to examine the effect of an educational intervention on the knowledge, attitude and practice of prescribing antimicrobial agents for upper respiratory tract infections (URTI) by residents in a teaching hospital setting. The groups participated in this study included resident physicians from the following departments: internal medicine, pediatrics, emergency, Ear, Nose, and Throat (ENT), and family medicine. All residents in the mentioned departments (118 residents) were offered a participatory approach in the research, however, only 69 agreed to take part. The involved residents were randomized using a computerized random-number generator into intervention (n = 37) and control (n = 32) groups (Figure 1).

Figure 1. Study design (flow chart showing participants' recruitment in the study).



The intervention group received an educational intervention that was implemented over a period of two weeks and consisted of two educational seminars covering topics related to the prescription of antimicrobial agents and resistance against them. In addition, each resident received a pocket-sized brochure which briefly summarized the main points of the full educational session to be placed in the clinic or used whenever needed. One seminar was given per week, and the seminars were presented for each department separately. It was clearly instructed that the educational intervention was carried out as part of a research project that required the intervention group not to share any information with the control group. The seminars discussed the approach to antimicrobial agents prescribing and dispensing according to the Centor criteria used in Jordan University Hospital [16], the American Family Physician guidelines for use of antimicrobial agents in acute URTIs [17], and the National Institute for Health and Clinical Excellence's (NICE) care pathway for respiratory tract infections [18]. The first seminar explained the guidelines for the consumption of antimicrobial agents and prescribing in adults; covering the management of the following conditions: acute bacterial sinusitis, pharyngitis, acute bronchitis, and viral infections such as influenza. The NICE's care pathway for the use of antimicrobial agents was also covered in the first session. The second seminar presented guidelines for antimicrobial agents prescribing for children and management of otitis media, acute bacterial sinusitis, pharyngitis, nonspecific cough illnesses such as bronchitis, and viral infections causing bronchiolitis were all discussed during the session. Strategies to help in minimizing the inappropriate use of antimicrobial agents were also provided in both seminars. Brochures provided for research participants were fully printed in color with easy to follow illustrations. The Centor criteria used in the hospital were also included in the brochures [16].

The control group did not receive any part of the intervention.

Before and after any interventions, all participating physicians in both intervention and control groups were asked to complete a 15 to 20 minutes online questionnaire after providing online consent of participation. The questionnaire measured the participants' knowledge, attitudes and behavioral intention towards antimicrobial agents' resistance and prescribing and was adapted according to the instrument developed and used by Liu *et al.* [19]. The questionnaire was validated to ensure content and construct validity, and reliability was calculated to Cronbach's alpha value of > 0.65 [19]. The baseline round of filling the questionnaire occurred before providing the educational intervention. The second round of filling the questionnaire was planned to occur three months post-intervention. In addition to filling the questionnaire, outpatient URTI antimicrobial agents' prescriptions for the two study arms were extracted from Jordan University Hospital's electronic medical records for the pre- and post-intervention periods. Pre-intervention period was considered to be from September to November 2019, and the post-intervention period to be the months February, March, and June 2020, respectively. For the post-intervention period, we excluded April and May since clinics were closed due to the COVID-19 pandemic. The study was approved by the Jordan University Hospital ethical review board (IRB).

The primary outcome of this randomized control study was to determine the outpatient antimicrobial agents prescribing rate for Upper Respiratory Tract Infections (URTIs). It was anticipated that there would be a decrease in antimicrobial agents prescribing following the educational intervention. The secondary outcome was to assess physicians' knowledge, attitude and behavioral intention toward antimicrobial agents prescribing and antimicrobial agents resistance. A questionnaire was used to assess this outcome and it included the following dimensions: attitude which included complacency (to prescribe antimicrobial agents for the satisfaction of patients), fear (to prescribe antimicrobial agents to avoid losing patients), ignorance (lack of interest in reducing antimicrobial agents prescribing to reduce antibacterial resistance), indifference (to lack any motivation to improve antimicrobial agents prescribing behaviors), and

Table 1. Baseline characteristics of research participants in the control (n = 32) and intervention (n = 37) groups (No significant differences existed at a *p*-value < 0.05 and valid percentages were calculated whenever missing values existed).

Research group	Control		Intervention	
	n	%	n	%
Gender				
Male	7	22.6	12	32.4
Female	24	77.4	25	67.6
Total	31	100.0	37	100.0
Specialization				
Emergency medicine	2	7.1	9	25.0
ENT	2	7.1	2	5.6
Family medicine	7	25.0	5	13.9
Internal medicine	12	42.9	11	30.6
Paediatrics	5	17.9	9	25.0
Total	28	100.0	36	100.0
Year of specialization				
First	9	29.0	10	27.0
Second	5	16.1	8	21.6
Third	6	19.4	7	18.9
Fourth	11	35.5	12	32.4
Total	31	100.0	37	100.0
Years of practice				
Less than 1	0	0.0	2	5.4
From 1 to 5	29	96.7	33	89.2
More than five but less than 10	1	3.3	1	2.7
More than 10	0	0.0	1	2.7
Total	30	100.0	37	100.0
Received training related to AB prescribing other than the study intervention				
Yes	4	13.3	9	24.3
No	26	86.7	28	75.7
Total	30	100.0	37	100.0
Age	Mean ± SD		Mean ± SD	
	27.6 ± 1.8		26.5 ± 4.6	

Table 2. Rates of antibiotic prescribing by the control and the intervention groups.

Rate of prescribing antibiotics for URTIs (number of prescriptions per 1,000 patients)	Control group	Intervention group	*p*-value
Pre-intervention	6.1	9.7	< 0.001
Post-intervention	5.1	11.6	< 0.001

responsibility avoidance (to believe that others are responsible for the problem of antimicrobial agents resistance). Behavioral intention included prescribing antimicrobial agents for upper respiratory tract infections, prescribing antimicrobial agents in general, and reducing antimicrobial agents prescriptions. Knowledge questions yielded overall knowledge score. Scoring was carried out according to the method described by Liu *et al.* [19].

The antimicrobial agents prescribing profiles retrieved from Jordan University Hospital's electronic medical records as well as data from the self-administered questionnaires were entered to the statistical software SPSS version 16 for further cleaning and analysis. Antimicrobial agents prescribing rates were calculated as number of prescriptions per 1,000 patients. Chi-square test was used to compare categorical variables while a t-test was used to compare continuous variables. For the statistical analysis, a *p*-value of less than 0.05 was considered significant.

Ethics statement

The study was approved by the Institutional Review Board in Jordan University Hospital, decision no. 255/2019.

Results

Of 118 residents invited to take part in the study, 69 agreed to participate and they were randomized into the intervention arm (n = 37) and the control arm (n = 32). Baseline characteristics of the two groups of research participants are shown in Table 1. There were no significant differences in baseline characteristics between participants in the intervention and the control groups.

At baseline and post-intervention, the rates of antimicrobial agents prescribed by the intervention group were significantly higher than those prescribed by the control group ($p < 0.001$) (Table 2). No significant differences in mean attitude, behavioral intention, and knowledge scores existed at baseline between the intervention and control groups (Table 3). Post intervention mean fear score (calculated from items 23-27 in the questionnaire) for the intervention group (mean ± SD of -0.83 ± 0.64) was significantly lower than mean fear score for the control group (mean ± SD of -0.75 ± 0.46; $p = 0.027$). Mean scores for all other attitude, behavioral intention, and knowledge dimensions did not change post-intervention significantly (Table 4).

Discussion

Up to the authors' knowledge, this is the first study to evaluate whether an educational intervention can improve antimicrobial agents prescribing behavior, knowledge, and behavioral intention of residents in a teaching hospital setting in Jordan. Previous literature from Jordan is limited to assessing the impact of educational interventions to improve the safe use of antimicrobial agents by the public rather than the prescribers [20]. Educational interventions targeting antimicrobial agents prescribing behavior present a promising approach in handling inappropriate antimicrobial agents prescribing and associated antimicrobial resistance. A relatively recent review by van der Velden *et al.* emphasized that the most effective

Table 3. Baseline attitude, behavioural intention, and knowledge calculated scores for the control and intervention groups (No significant differences existed at a *p*-value < 0.05).

Groups	Control		Intervention	
	mean	SD	mean	SD
Attitude				
Complacency	-1.19	0.64	-1.11	0.74
Fear	-0.75	0.52	-0.84	0.59
Ignorance	1.50	0.44	1.64	0.48
Indifference	0.71	0.48	0.72	0.62
Responsibility avoidance	1.18	0.46	1.32	0.41
Behavioural intention				
Prescribe antibiotics for upper respiratory tract infections	2.90	1.97	3.00	2.13
Prescribe antibiotics	-0.30	0.99	-0.40	0.86
Reduce antibiotic prescriptions	1.26	0.68	1.29	0.71
Knowledge	0.61	0.14	0.62	0.14

interventions aiming at decreasing overall prescribing included educational material provided for the physicians [21]. In another study, Wei *et al.* demonstrated in a cluster randomized controlled trial that healthcare providers perceived training courses and repeated meetings with senior physicians as useful in improving their antimicrobial agents prescribing behavior [22]. Additionally, in an interventional study by Deuster and *et al.,* teaching and implementing treatment guidelines for nosocomial infections increased the rates of proper antimicrobial agents prescribing with the resultant improvement in patient care [23].

The study included residents from five specializations within which antimicrobial agents can be prescribed for URTI. The specializations were: internal medicine, pediatrics, emergency, Ear, Nose, and Throat (ENT), and family medicine. Similarly, in a systematic review by Roque *et al*., it was observed that most studies included in the review had physicians as their main target for the educational interventions aiming to improve antimicrobial agents use [24].

One important finding of the current research was the relatively small proportion of residents who received specialized education regarding antimicrobial agents prescribing before the study (13.3% of the control group and 24.3% of the intervention group). The need for additional education on antimicrobial agents prescribing was emphasized among physicians included in the study by Zhu *et al*. as a way to rationalize antimicrobial agents use [25]. Moreover, Pulcini and Gyssens pointed out that in many countries, physicians receive their specialized antimicrobial agents education at a relatively late phase of their practice, while it is suggested to be more effective in their early years of training [26]. Therefore, findings of the current study in addition to the existing literature highlight the need for education of physicians in antimicrobial stewardship as early as possible in their training journey.

The effectiveness of the educational intervention provided in the current study was evaluated by comparing the rates of antimicrobial agents prescribed by the residents in the control and intervention groups. At baseline and post-intervention, the rates of antimicrobial agents prescribed by residents in the intervention group were higher than those by the control group. However, based on the CONSORT 2010 statement, it is not recommended to report baseline significance testing as they can be misleading [27]. Hence, discussion of the findings of the current study will only be limited to significant differences in post-intervention.

Post-intervention, the rate of antimicrobial agents prescribing was significantly higher for the intervention group (11.6 prescriptions per 1,000 patients) than the control group (5.1 prescriptions per 1,000 patients), which indicates failure of the educational intervention in improving antimicrobial agents prescribing practices. On one hand, similar results of the failure of educational interventions in improving antimicrobial agents prescribing behaviors were reported by a considerable body of literature [28-31]. Suggested reasons for such failure included the continued belief in the effectiveness of antimicrobial agents and a desire for a rapid response, low intensity of the interventions provided, and difficulties in changing the behavior of physicians in spite of being aware of the best practice [29-31]. On the other hand, findings of this study might be attributed to a different factor, which is the COVID-19 outbreak. As mentioned earlier, the post-intervention period included a two-month gap, in which clinics were closed due to the COVID-19 outbreak. Therefore, the researchers had to consider February, March, and June instead of February, March, and April as the post-intervention phase. The surge of antimicrobial agents prescribing in the post-intervention period of the

Table 4. Post-intervention attitude, behavioural intention, and knowledge scores for the control and intervention groups.

Groups	Control		Intervention	
	mean	SD	mean	SD
Attitude				
Complacency	-1.23	0.62	-1.19	0.55
Fear *	-0.75	0.46	-0.83	0.64
Ignorance	1.73	0.44	1.73	0.37
Indifference	0.77	0.59	0.80	0.67
Responsibility avoidance	1.33	0.43	1.33	0.38
Behavioural intention				
Prescribe antibiotics for upper respiratory tract infections	2.25	1.11	3.00	1.83
Prescribe antibiotics	-0.39	0.80	-0.42	0.70
Reduce antibiotic prescriptions	1.30	0.62	1.28	0.59
Knowledge	0.61	0.15	0.64	0.18

* Significant difference in fear scores, $p = 0.027$ (No significant differences existed at a p-value < 0.05 for all other variables).

current research might be the result of trying to control certain clinical presentations that were believed to be associated with COVID-19 infection. Since not all patients coming to the included clinics were necessarily tested for COVID-19 viral infection, this implied that there was a possibility of treating infected patients. In light of the lack of guidelines on the use of antimicrobial agents for treatment of COVID-19 at that time, residents possibly had to prescribe antimicrobial agents to control the symptoms that were assumed to be related to COVID-19 infection. Similarly, Beović *et al.* reported that physicians prescribed antimicrobial agents based on patients' symptoms rather than laboratory tests and radiology [32]. Recent evidence from different parts of the world suggests that although only a small proportion of COVID-19 patients developed secondary infections requiring antimicrobial agents therapy, a large proportion of those patients received antimicrobial agents [33-35]. Several reasons for this phenomenon have been reported in the literature including overloaded laboratories that can cause delays in processing microbiological samples and the absence of antiviral treatments with proven efficacy [34]. Consequently, it cannot be clearly concluded whether the educational intervention provided in this study actually failed in changing the antimicrobial agents prescribing behavior of the involved residents or that results of the research were affected by the COVID-19 outbreak. Therefore, it is recommended to carry out further research to explore the underlying factors that might have affected the reported outcomes. Qualitative research including a sample of residents from the clinics included in the current study is recommended in this context.

Among different attitudes that were explored in this study including behavioral intention and knowledge dimensions, only fear scores showed a significant difference between control and intervention groups post-intervention. After receiving the education, mean fear scores for the intervention group were significantly lower than mean fear scores for the control group. This implies that after receiving the educational intervention, residents in the intervention group seemed less concerned about losing patients or adversely affecting them when they do not prescribe unnecessary antimicrobial agents. This outcome indicates a favorable effect of the educational intervention on the attitudes of residents prescribing antimicrobial agents for URTI. However, the educational intervention failed to achieve a significant impact on all other attitudes, behavioral intentions, and knowledge dimensions. Similarly, the failure of the educational intervention provided for physicians in improving knowledge and attitudes towards better use of antimicrobial agents was reported by another study conducted by Stille *et al.* [36]. On the contrary, a positive impact of educational interventions on the attitudes and beliefs of physicians were reported by other researchers [37,38]. As mentioned earlier, the occurrence of the COVID-19 outbreak during the study period may have caused a state of confusion or uncertainty among research participants. This in turn might have interfered with the effect of the education received as part of this study and had an effect on the reported outcomes.

Study limitations

This study had a number of limitations. First, it was limited to a single teaching hospital setting, which might hinder the generalization of the results to other larger-scale studies. Secondly, the COVID-19 outbreak led to the closure of the clinics included in the study for two months, which caused some disturbance to the post-intervention period and might have influenced the research findings.

Conclusions

While a large body of evidence supports the use of educational interventions as a tool to improve antimicrobial agents prescribing behaviors, this did not apply to findings of this study. The educational intervention provided for residents in the current research had a positive effect on one dimension of the attitude of included residents, and this was a fear of losing patients or it was negatively affected by the condition that no antimicrobial agents were going to be prescribed. However, the intervention failed to improve all other dimensions of attitude, behavioral intention, and knowledge. Most importantly, the intervention failed in improving antimicrobial agents prescribing behaviors of the included residents expressed as prescribing rates. Results of this study are thought to be the reason of the occurrence of the COVID-19 outbreak during the study period, which caused a state of confusion or uncertainty among research participants. These findings are worth further exploration, which can be achieved by expanding on the current findings using qualitative research methods.

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Author contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were

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