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Research Paper

Antibiotics use and appropriateness in two Jordanian children hospitals: a point prevalence study

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Abstract

Background Although inappropriate antibiotics prescribing in hospitals is a key factor in accelerating antibiotic resistance, inadequate data are available about antibiotics prescribing rate and appropriateness. Our study aimed to measure antibiotics prescribing rate, indications, appropriateness and predictors.

Methods The study was conducted in two public children hospitals (five wards) in Jordan using one-week point prevalence survey to prospectively collect the data. Appropriateness of antibiotics therapy was assessed by a multidisciplinary committee and predictors of inappropriate prescribing were studied through multivariate logistic regression.

Key findings The overall antibiotics prescribing rate was 75.6% (n = 501/663), where the highest rate of antibiotics prescribing was in the Pediatrics ward (82.2%, n = 222/270). However, the lowest rate was in the Pediatric Intensive Care Unit (30.0%, 9/30). The most common antibiotics classes prescribed were: Beta-lactams (57.5%, n = 492/855). The most common underlying condition for antibiotics prescribing was upper respiratory tract infections (25.5%, n = 128/501) followed by pneumonia (20.6%, n = 103/501). Around half of antibiotics were prescribed upon appropriate decision (49.5%, n = 423/855). However, 22.0% (n = 188/855) of antibiotics were wrongly chosen, and 9.5% (n = 81/855) were wrongly applied. Initially inappropriate decision for prescription occurred in 15.3% (n = 131/855) of antibiotics. Ceftriaxone (OR 3.1; 95% CI 2.6–4.1; P = 0.03) and patients with ≥3 medication orders (OR 2.6; 95% CI 1.7–3.5; P = 0.001) significantly predicted inappropriate antibiotics prescribing.

Conclusions The incidence of antibiotics prescribing in Jordanian children hospitals was high compared to other countries. Further multi-centric studies are required to enhance the generalisability of results and better develop effective and efficient antibiotic stewardship programmes.

Keywords: Health services research; antibiotic appopriatness; pediatric setting; Jordan

Introductionr

The world has witnessed a growing rate of antibiotic resistance (ABR) over the past 50 years.[1] The costs of ABR are with a high burden, as it is responsible for around 700 000 deaths annually, with an expectation to rise to 10 million deaths in 2050. Consequently, the world economy status that is resembled in its gross domestic product will drop by 3.5% during the next three decades, and is the hardest to the poorest countries.[2] Novel antibiotics have been discovered rarely which urged the World Health Organization (WHO) to announce ABR as an imminent threat to the public health.[3, 4] In the developing countries, the cure of some common diseases in pediatrics become challenging due to the spread of ABR.[5] Misuse of antibiotics includes inappropriate prescribing and overprescribing of antibiotics leading to dramatic increase of ABR and emergence of resistant pathogens.[6–12] The use of broad spectrum antibiotics increased in the 1990s multiplying the ABR issue.[13, 14] These practices are results of poor enforcement of regulations controlling rational use of antibiotics, selling antibiotics without prescriptions, and self-medication. Regulations controlling pharmaceutical marketing of broad-spectrum antibiotics are lacking. Also, awareness of public on rational use of antibiotics and poor training of medical staff on ABR are challenges for implementing antimicrobial stewardship programmes.[2] A study conducted in India (2018), approached the ethical challenges among physicians when prescribing antibiotics. One interesting issue was that physicians were driven by the need to fulfil patients' expectations to achieve instant results.[15] Antimicrobial stewardship programmes (ASPs) can be effective in developing interventional measures, which have an important role in controlling ABR.[16, 17] A study conducted in a humanitarian surgical hospital in Jordan, found that antibiotic use was significantly reduced when implementing antibiotic stewardship program over a year-period of time.[18] However, sufficient data about antibiotics prescribing appropriateness are needed to build effective and efficient approaches for ASPs.[19]

Overall, antibiotics prescribing rate was found to be high especially in pediatrics wards in the hospitals of Australia, Turkey, USA, Vietnam, Scotland, Canada, Italy, Denmark, France, Switzerland, and 20 other European countries.[20–31] In the USA, antibiotics are the most commonly prescribed medications among hospitilised patients, as more than half of patients were given at least one dose of an antibiotic between 2006–2012.[32] In Australia, 28% of patients on antibiotics were given at least one prescription that was considered to be inappropriate.[19] Another Australian study showed that antibiotics were prescribed for 32.4% of surveyed patients; 14.5% of which were judged as inappropriate.[33] One more Australian study showed that 47% of antibiotics were prescribed inappropriately.[34] The rate of antibiotics prescribing in Turkey was 54.6% and around half of patients on antibiotics were given at least one inappropriately prescribed antibiotics.[35] Consistently, a study conducted in Jordan revealed that more than half (54.1%) of the antibiotics were prescribed in an off-label pattern among admitted pediatrics in NICUs and (46%) in pediatric wards, Such a pattern of prescribing includes the use of licensed medicines outside their license in terms of recommended dose, recommended indication, recommended age and recommended route, leading to reported fatalities[36] In developing countries, failure to adhere to the guidelines coupled with lack of awareness of the health hazards associated with inappropriate use of antibiotics are expected.[37–40] Many studies conducted recently in Jordan to investigate medication safety in community and hospital settings have found a high rate of irrational dispensing and prescribing of medications[41–46]

Among all studies conducted in Jordan, this study was the first study to investigate antibiotics prescribing rate and appropriateness in two Jordanian children hospitals using a point prevalence survey.

Method

Study design and setting

A point prevalence study on antibiotics use in two Jordanian children hospitals was conducted to assess the frequency, indications, guidelines compliance and characteristics of antibiotics prescribing. Five pediatrics wards from two Jordanian public hospitals were included in our study. In each ward, a week point prevalence study was carried out between October and November 2019. Our study was conducted in the Gynecology and Pediatric Hospital [Neonatal Intensive Care Unit NICU (80 beds), and Pediatric Intensive Care Unit PICU (10 beds), and Pediatrics ward (94 beds)] and the Surgery Hospital [Pediatric Surgery ward (25 beds) and Surgery Intensive Care Unit SICU (10 beds)].

Data collection

Senior clinical pharmacists were trained to collect data through providing an information pack and training session prior to the survey. Data were collected from all inpatients being prescribed at least one antimicrobial at the time of chart review. The clinical pharmacists had access to the admission and progress notes, surgical notes, medication charts, and pathology and microbiology results. All neonatal and pediatric patients, admitted to the ward, taking at least one antibiotic by any route of administration was included. A standard checklist was used to collect the data from the patient documents such as age, sex, diagnosis, the class of the prescribed antibiotics and reason for prescribing.

Appropriateness evaluation

Appropriateness of antibiotic therapy was assessed by multidisciplinary committee: a consultant pediatrician, an infectious diseases pharmacotherapist and a clinical pharmacist, who reviewed clinical information against the red book,[47] and internal antibiograms of included hospitals; antimicrobial selection, dose, frequency, duration (for prophylaxis prescriptions only), hypersensitivity contraindication and microbiology investigation results (including antibiotic susceptibilities of any identified pathogens) were considered by the assessors. Standardised terminologies were adopted from a previous study[19] to describe appropriateness. The Kappa statistic was used to test interrater reliability. The Kappa can range from −1 to +1. Value of kappa Below 0.5 was considered as bad reliability, between 0.5 and 0.7 moderate reliability, between 0.7 and 0.8 good, and above 0.8 great reliability.[48]

Data analysis

Data were coded and entered into SPSS V24 by the investigator. Descriptive statistics were computed for the study variables. Frequency distribution tables were used to describe the findings and graphs were plotted.

Multivariate logistic regression was conducted to find which predictors were significant. Independent variables were: the ward (NICU, PICU, Pediatrics, Surgery ICU and Pediatric Surgery), present illness of patients on ABs, antibiotic (for reliable outcomes, antibiotics prescribed less than 10 times during the survey were combined together in a group called 'Others'), and number of medications prescribed per patient. Dependent variable was appropriate/

inappropriate antibiotics prescribing (inappropriate decision, choice and application were combined). Insufficient information cases were excluded from the regression test. Only significant variables were discussed in results. Adjusted odds ratio and *P* values for each model at 95% confidence interval were calculated using Statistical Package for the Social Sciences (SPSS).

Results

Of 663 neonatal and pediatric patients admitted during the study, 75.6% (n = 501/663) were prescribed at least one antibiotic. The highest rate of antibiotics prescribing was in the Pediatrics ward 82.2% (n = 222/270) and the lowest rate was in the PICU (30.0%, 9/30) (Figure 1).

Of the 501 patients who received antibiotics, 46.7% (n = 234/501) were <1 month-old and 21.6% (n = 108/501) were 1–6 months. For patients who were on antibiotics therapy, the mean length of stay at the hospital was 2.9 days, the mean age was 2.1 years and the mean weight was 5.4 Kg (Table 1).

Overall, 855 antibiotics were prescribed. The majority of antibiotics were Beta-lactams (57.5%, n = 492/855) and Aminoglycosides (22.5%, n = 192/855). Macrolides were prescribed for nine patients and colistin for six patients only (Figure 2). Our results showed that more than half of prescribed antibiotics (53.7%, n = 459/855) were given for more than three days (Table 2)

The majority of patients were prescribed antibiotics for upper respiratory tract infections (25.5%, n = 128/501), pneumonia (20.6%, n = 103/501), urinary tract infections (16.6%, n = 83/501) and sepsis (13.4%, n = 67/501). More details about patients underlying conditions are illustrated in Figure 3.

As shown in Table 3, more than two thirds of antibiotics (82.2%, n = 703/855) were prescribed upon appropriate decision, of which 49.5% (n = 423/855) were completely appropriate (correct choice of antibiotic and correct application), 22.0% (n = 188/855) with wrong antibiotic choice, 9.5% (n = 81/855) with wrong antibiotic application, and 3.7% (n = 32/855) with little or no information about the choice or the application of antibiotics. Initially inappropriate decision for prescription occurred in 15.3% (n = 131/855) of antibiotics.

The highest rate of completely appropriate antibiotics choice was found in the Pediatric Surgery 61.3% (n = 57/93) and the lowest one was recorded in the PICU 38.5% (n = 10/26) (Figure 4). The rate of antibiotics inappropriate choice ranged between 15.2% and 26.8% where the highest rate recorded in the NICU.

Predictors of inappropriate antibiotics prescribing were ceftriaxone antibiotic {odds ratio (OR) 3.1; 95% Connfidence interval (CI) 2.6–4.1; P = 0.03} and patients with ≥3 medication orders {OR 2.6; 95% CI 1.7–3.5; P = 0.001}.

Discussion

Although inappropriate prescribing of antibiotics has had catastrophic consequences on patient safety, economy and development of an efficient healthcare system, it has continued to be a widespread

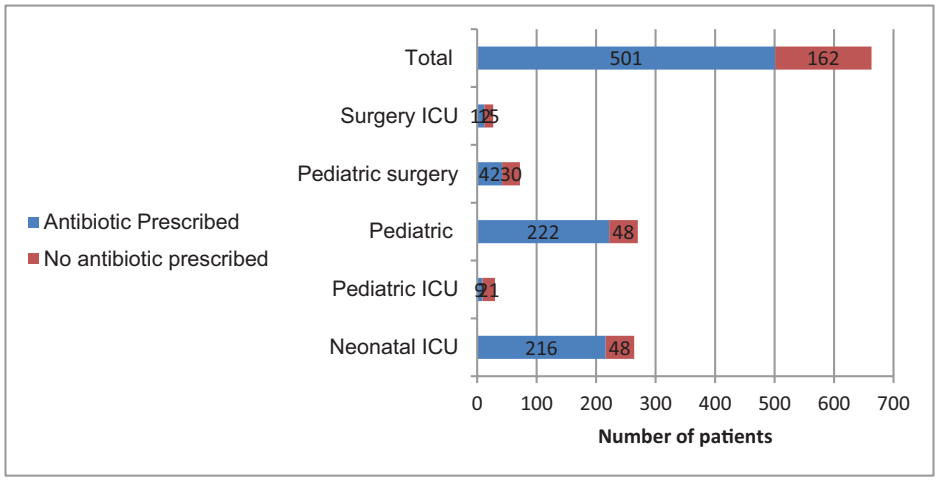

Figure 1 Proportion of patients (n = 663).

Table 1 Characteristics of patients prescribed antibiotics

Hospital name	Ward	Number of beds	hospitalised patients	Patients on antibiotics therapy	Mean age of patients on antibiotics therapy (Years)	Mean weight of patients on antibiotics therapy (Kg)	Mean number of medications for each patient	Mean length of stay for patients on antibiotics therapy (Days)
Gynecology and Pediatric Hospital	Neonatal ICU	80	264	81.8% (n = 216/264)	0.4	2.1	2.4	2.4
	Pediatric ICU	10	30	30.0% (n = 9 /30)	2.3	4.8	3.6	3.6
	Pediatrics	94	270	82.2% (n = 222 /270)	2.7	7.6	2.9	4.1
Surgery Hospital	Pediatric Surgery	25	72	58.3% (n = 42/72)	1.2	4.1	4.3	3.2
	Surgery ICU	10	27	44.4% (n = 12/27)	3.9	8.3	3.2	1.4
Total		**209**	**663**	**75.6% (n = 501/663)**	**2.1**	**5.4**	**3.3**	**2.9**

practice. These uncontrolled behaviours occurring mostly in hospitals are responsible for developing resistant pathogens. Our study aimed to assess the rate of antibiotics prescribing, uses, and appropriateness in five pediatrics wards of two Jordanian public hospitals using one-week PPS.

Our study results could not be generalised as it was conducted in two hospitals only; however, our findings would shed light on irrational practice of antibiotics prescribing among Jordanian hospitals. In addition, the study could assess the accuracy and efficiency of using protocols in the inpatient settings as our data included information about patients' profile, culture and sensitivity tests, type of the treatment and type of the infection. Fortunately, Jordanian Ministry of Health is paving the road towards implementation of the Global Antimicrobial Resistance Surveillance System (GLASS). Yet, there is no resulted data as surveillance is still ongoing.[2] Some limitations appear constrain the study. The lack of specific pediatric guidelines for empirical antibiotics treatment, as well as for standards to guide a timely collection of appropriate microbiological specimens. The limited number of hospitals and only inpatient departments were covered. As there is a scarce of outpatient follow-up studies to detect antibiotic-use patterns. Moreover, the duration of the study was short, thus it cannot be generelised.

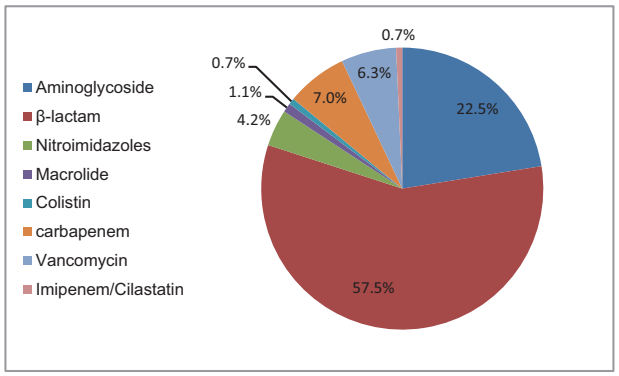

Figure 2 Classes of antibiotics prescribed (n = 855).

Our findings showed a high rate of antibiotics prescribing in Jordanian neonatal and pediatric units, with 75.6% overall rate. This was closely consistent with studies from Vietnam (67.4%) and Canada (70–79%);[9, 25] however, it was markedly higher than other rates from Australia (46%), Europe (35%), Turkey (54.6%), Italy (43.9%), Netherlands (33.8–36%), France (40.9%), Switzerland (44.4%), and Scotland (30.2%). [20–22, 24–31, 49]. Other studies conducted in South Africa and Pakistan showed higher antibiotics prescribing rates than ours with 92% and 100%, respectively.[50, 51]

Many factors may have contributed to the variation in prescribing rates between studies, such as: geographic locations, prevalence of infections and adherence of medical professionals to the guidelines. Our results showed that 46.7% (n = 234/501) of patients on antibiotics therapy were <1 month old and 21.6% (n = 108/501) were <6 months. Our results were consistent with other studies.[19, 28], in which high infection incidence was evident in this age group. In general, our results reflected a high incidence of broad-spectrum antibiotics prescribing in Jordanian pediatric hospitals. Third generation cephalosporins and carbapenems, which are recognised drivers for ABR, accounted for a considerable number of prescribed antibiotics.

Our study showed that the Pediatrics ward and NICU had markedly higher patterns of antibiotics prescribing compared to the PICU and Pediatric Surgery wards. These findings reflected the difference in medical specialty, the paucity of evidence regarding antimicrobial prescribing for many childhood infections and different local patterns of antimicrobial resistance. Our results were consistent with a previous study conducted in Australia.[19]

Our results confirmed the high proportion of empirical antibiotics prescriptions similar to the literature.[9, 19] Our findings highlighted the challenge in obtaining high-quality microbiological

Table 2 Characteristics of prescribed antibiotics

Antibiotic (antibiotics) name	Frequency (n, %)	Route		Type of treatment					Duration (days)	
		IV	PO	Empirical	Definitive treatment (positive culture)	Prophylactic surgery	Prophylactic medical	Both empirical and prophylactic	<3 days	≥3 days
Ampicillin	(201, 23.5%)	201	0	90	33	9	24	48	93	108
Gentamicin	(171, 20%)	171	0	96	21	12	6	36	96	75
Ceftriaxone	(144, 16.84%)	144	0	42	12	27	3	60	27	117
Ceftazidime	(99, 11.6%)	99	0	33	12	9	9	36	75	24
Meropenem	(60, 10.81%)	60	0	27	3	9	6	15	33	27
Vancomycin	(54, 6.32%)	54	0	12	12	3	9	18	21	33
Cefotaxime	(48, 5.61%)	48	0	12	0	9	12	15	12	36
Metronidazole	(36, 4.21%)	35	1	12	6	6	3	9	24	12
Amikacin	(18, 2.1%)	18	0	6	0	3	9	0	6	12
Azithromycin	(9, 1.05%)	9	0	3	6	0	0	0	3	6
Imipenem/ Cilastatin	(6, 0.7%)	6	0	3	3	0	0	0	3	3
Colistin	(6, 0.7%)	6	0	3	0	0	0	0	0	3
Tobramycin	(3, 0.35%)	3	0	0	3	0	0	0	3	0
Total	(855, 100%)	(854, 99.9%)	(1, 0.1%)	(339, 39.6%)	(111, 13.0%)	(87, 10.2%)	(81, 9.5%)	(237, 27.7%)	(396, 46.3%)	(459, 53.7%)

IV: intravenously; PO: oral

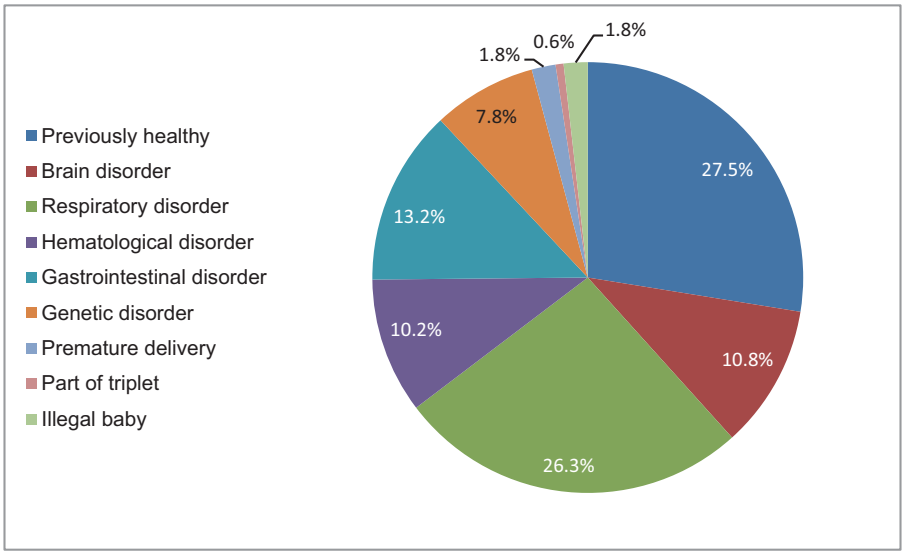

Figure 3 Comorbidities of patients on antibiotics (n = 501).

Table 3 Appropriateness of antibiotics prescribing (n = 855)

Ward	Appropriate decision				Inappropriate decision
	Complete appropriate	Inappropriate choice	Inappropriate application	insufficient information	
Neonatal ICU	42.3% (n = 164/388)	26.8% (n = 104/388)	10.6% (n = 41/388)	4.9% (n = 19/388)	15.4% (n = 60/388)
Pediatric ICU	38.5% (n = 10/26)	19.2% (n = 5/26)	15.4% (n = 4/26)	3.8% (n = 1/26)	23.1% (n = 6/26)
Pediatrics	57.1% (n = 173/303)	15.2% (n = 46/303)	6.9% (n = 21/303)	3.0% (n = 9/303)	17.8% (n = 54/303)
Pediatric Surgery	61.3% (n = 57/93)	22.6% (n = 21/93)	8.6% (n = 8/93)	1.1% (n = 1/93)	6.4% (n = 6/93)
Surgery ICU	42.2% (n = 19/45)	26.7% (n = 12/45)	15.5% (n = 7/45)	4.4% (n = 2/45)	11.1% (n = 5/45)
Total	**49.5% (n = 423/855)**	**22.0% (n = 188/855)**	**9.5% (n = 81/855)**	**3.7% (n = 32/855)**	**15.3% (n = 131/855)**

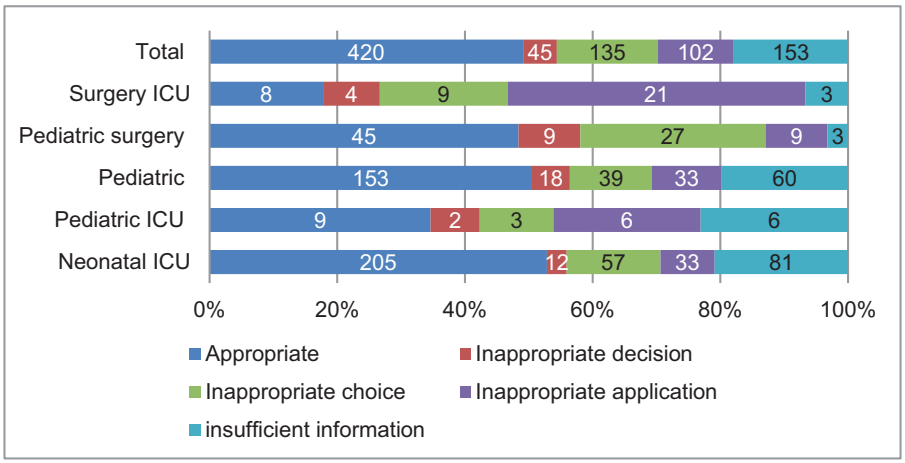

Figure 4 Appropriateness of antibiotic prescribing (n = 855).

samples before prescribing antibiotics in children and the low priority placed on ideal specimen collection in some contexts. These factors emphasise the need for specific pediatric guidelines for empirical antibiotics treatment and for standards to guide timely collection of appropriate microbiological specimens.

Around half of the prescribed antibiotics were judged as completely appropriate. Results in the literature are widely affected by geographic location, nature of the targeted ward and to some extent the reference guidelines. Moreover, the opinions of the assessors have a big impact on the variation of results; that is, the proportion of antibiotics prescriptions deemed appropriate varied depending on the assessor's specialty: intensivists judged 82% appropriate; infectious diseases physicians 69%, and pharmacists 45%.[9] To overcome this problem, we used the interrater reliability test to measure

internal consistency between judges and raters' judgments were close to each other by 84% agreement. Therefore, the consistency between raters was strong.

Our results showed that around one third of antibiotics were deemed as 'inappropriate choice' and 'inappropriate application'. Many factors may explain our findings; for example, lack of pharmacotherapy knowledge of prescribers, work overload and low staff number in a hurried environment, such as the NICU and PICU.

Our results showed clear difference in appropriateness categorisation among the included pediatrics wards, where the highest rate of appropriate decisions was in the Pediatric Surgery. On the other hand, the highest rates of inappropriate choice and inappropriate decision were recorded in the PICU. These results call for further investigation on the appropriateness of antibiotics prescribing in children hospitals, to explore the root causes of this serious problem.

Our findings highlighted the relationship between certain antibiotics and the occurrence of inappropriate prescribing; ceftriaxone was around three times more likely to be prescribed inappropriately than other antibiotics. Besides the common belief among healthcare professionals in Jordan that ceftriaxone has a wide margin of safety and higher efficacy than other antibiotics, poor adherence to the guidelines might have led to this outcome.

In summary, antibiotics were prescribed frequently in two pediatric hospitals in Jordan, a significant percentage of these prescribing decisions were inappropriate, and around half of the antibiotics were prescribed empirically. A large-scale multi-centric study to investigate antibiotics prescribing appropriateness in different hospital settings is necessary to enhance the generalisability issue and provide clear insight toward the current situation of antibiotics prescribing practice in Jordan.

Conclusion

Our Study showed higher rate of antibiotics prescribing in children hospitals compared to other countries. Many of the antibiotics were prescribed inappropriately and there was a clear difference in rate and appropriateness of antibiotics prescribing between different children wards. Efficient and reliable antibiotics stewardship strategies and plans are required to enhance patient safety and minimise the risk of ABR.

Author contributions

D.H.A.-Q.: study design development, conceptualization, data collection, data analysis, summarization, and results' interpretation and manuscript drafting. N.S.I., A.A. and A.A.E.-S.: proposal writing and polishing, Data collection, statistical analysis, results interpretation, work design manuscript write up, reviewing and proof reading. M.S.A., R.I. and H.A.A.-Q.: proposal polishing, data collection, data analysis manuscript critical appraisal, review analysis and proof reading. S.H., N.A.M. and O.M.I.: literature review, data analysis, proposal review, manuscript review and polishing and critical appraisal.

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Conflict of Interest

None declared.

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