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Original Article

Investigating antibiotic use in Gaza Strip hospitals: A retrospective cross-sectional analysis

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Abstract

Introduction: Rates of antimicrobial resistance in the Gaza Strip are rising while regulations on antibiotics use are weakly implemented. This study aimed to investigate antibiotic use in hospitals utilizing World Health Organization (WHO) hospital, prescribing, and patient care indicators.

Methodology: A retrospective study was conducted at Al Shifa medical complex (SMC), Nasser Medical Complex (NMC), and European Gaza Hospital (EGH). Data for hospital indicators were collected from drug inventory records and by interviewing hospital pharmacy managers, while data for prescribing and patient care indicators were collected from medical records from all departments. WHO standard data collection forms and formulas to calculate quantitative indicators were used.

Results: Standard treatment guidelines for infectious diseases were unavailable. The availability of key antibiotics on the day of the investigation was 58.62%, 90.9%, and 44.82%, and antibiotics were out of stock for 120.5, 63.3, and 119.8 days/year in SMC, NMC, and EGH, respectively. A total of 1400 patients' records were screened; 68.2% of patients were prescribed antibiotics with an average duration of 3 days. The number of antibiotics prescribed was 1.26/hospitalization, 55% were prescribed by generic name, 98% were consistent with the essential medicine list, and 94.7% were given parenterally. Ceftriaxone was the most commonly used antibiotic (47.5%). Adherence rates to STGs for Caesarean section antibiotic prophylaxis and for pneumonia were 43% and 6.3%, respectively. About 97% of doses of prescribed antibiotics were administered and patients on antibiotics stayed in the hospital for 4.1 days.

Conclusions: Antibiotic utilization patterns are less than optimal. Strategies to improve antibiotic use in the investigated hospitals are needed.

Key words: Antibiotics; WHO indicators; resistance; prescribing; hospital.

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Introduction

The discovery of antibiotics was a major milestone in the history of medicine and human health. Antibiotics have enabled us to control bacterial infections that were a leading cause of death and thus have led to a significant decrease in morbidity and mortality [1]. However, this situation has changed dramatically due to the emergence of antimicrobial resistance (AMR), which has become a major public health threat in the 21st century [2]. Infections with AMR strains lead to serious illnesses, an increase in hospital admissions, prolonged hospital stays, accelerated healthcare costs, and most importantly, an increased likelihood of treatment failures and deaths [3]. A recent systematic analysis estimated that in 2019; 4.95 million deaths were associated with drug-resistant infections, of which 1.27 were directly attributable to AMR [4]. An earlier review of AMR by the UK government estimated that, by 2050, AMR could kill 10 million people every year if proper actions were not taken [2]. In Europe, AMR is associated with losses of more than 9 billion euros/year [5], while in the USA, AMR adds a 20 billion dollars surplus in direct health care costs [6].

Misuse of antibiotics is a major factor that accelerates the rate of AMR worldwide [7]. This problem is common in hospitals, especially in developing countries where 79%-84% of patients are prescribed antibiotics [8-10]. Antibiotic misuse in hospitals includes over-prescription of antibiotics, overuse of injectable antibiotics, prolonged or very short durations of treatments, subtherapeutic dosing, overuse of broad-spectrum antibiotics or broad-spectrum combinations, and poor adherence to standard treatment guidelines (STGs). Alarming rates of antibiotic misuse in hospitals have been reported in developing countries [11]. Lack of accurate drug information, weak training of medical graduates, absence of continuing education programs, poor diagnostic facilities, poor communication and

coordination among health care practitioners, and poor regulations and policies are possible causes of antibiotic misuse [12].

In 1993, the World health organization (WHO) published the manual "How to Investigate drug use in health facilities" which includes 12 indicators to assess drug use in outpatient settings [13]. In 2012, the manual "How to investigate Antimicrobial Use in Hospitals: Selected Indicators" was released to complement the original WHO indicators and address antimicrobial use in the inpatient setting. The manual was developed under the Rational Pharmaceutical Management Plus Program of Management Sciences for Health and revised under the Strengthening Pharmaceutical Systems Program [14]. This manual has been instrumental in standardizing antibiotic use studies in developing countries. It presented 16 indicators: five hospital-related, nine prescribing indicators, and two related to patient care medicine use in inpatient health facilities. Many studies from developing countries have reported using those indicators to assess antibiotic use in different healthcare settings [8,9,15,16]. Yet, no similar studies have been published from Palestine (West Bank/Gaza Strip). Considering that rates of AMR in the Gaza Strip are rising to dangerous levels [17] and that regulations on the use of antimicrobials are poorly implemented, a thorough exploration of antibiotic use became mandatory to identify weaknesses in practice and to develop interventions to improve antibiotic utilization in our hospitals. Therefore, this study aimed to investigate antibiotic management problems in Gaza Strip hospitals using WHO hospital indicators, as well as antibiotic prescribing and administration patterns using WHO prescribing and patient care indicators.

Methodology

Study design and setting

This is a retrospective cross-sectional study that was carried out at the main government hospitals in the Gaza Strip: Al-Shifa medical complex (SMC), European Gaza Hospital (EGH), and Nasser Medical Complex (NMC). It assessed three antibiotic use indicators (hospital, prescribing, and patient care indicators) (Table 1). The study adhered to the WHO methodology and used the recommended data collection forms and methods for the calculation of quantitative outcome indicators [14]. The antibiotic assessment covered the period between 1st January 2018 and 31st December 2018. Data were collected over 6 months between July 2019 and January 2020.

Data collection

Hospital indicators

Hospital indicators assessed in this study are listed in Table 1. Data on hospital indicators 1, 2, and 3 reflects current situation (at the time of investigation), while data for hospital indicator 4 covered the year 2018. The most recent copies of the essential medicine list (EML), key antibiotics, and standard treatment guidelines (STGs) were obtained from the pharmacy departments in the three hospitals. Data for hospital indicators were collected by interviewing pharmacy managers and by reviewing hospital pharmacy drug inventory records. All extracted data were reported on the standard WHO data collection forms (instruments) (Supplementary Tables 1, 4, 5).

Prescribing and Patient care indicators

For prescribing and patient care indicators (Table 1), data from medical records of patients admitted during the year 2018 were collected. According to the

Table 1. WHO indicators for investigating antimicrobial use in hospitals used in the study [14].

No.	***Hospital indicators***
1.	Existence of standard treatment guidelines (STGs) for infectious diseases
2.	Existence of an approved hospital formulary list or essential medicines list (EML)
3.	Availability of a set of key antibiotics in the hospital stores on the day of the study
4.	Average number of days that a set of key antibiotics is out of stock
No.	***Prescribing indicators***
1.	Percentage of hospitalizations with one or more antibiotics prescribed
2.	Average number of antibiotics prescribed per hospitalization in which antibiotics were prescribed
3.	Percentage of antibiotics prescribed in consistency with the hospital formulary list
4.	Average duration of prescribed antibiotic treatment
5.	Percentage of patients who receive surgical antibiotic prophylaxis for cesarean section in accordance with hospital guideline
6.	Average number of doses of surgical antibiotic prophylaxis prescribed for cesarean section procedures
7.	Percentage of patients with pneumonia who are prescribed antibiotics in accordance with standard treatment guidelines
8.	Percentage of antibiotics prescribed by generic name
No.	***Patient care indicators***
1.	Percentage of doses of prescribed antibiotics actually administered
2.	Average duration of hospital stay of patients who receive antibiotics

WHO methodology, the minimum number of records that should be taken from each hospital is 100. In this study, 300 records for patient care indicators and prescribing indicator numbers (1, 2, 3, 4, and 8) were taken from different departments in each hospital. This was done to minimize bias and to provide a better assessment of antibiotic use. In the 3 hospitals, medical records are usually kept in the medical archive. The archiving system is computerized and medical records can be sorted by date of admission, departments, or by type of disease. The 300 records from each hospital were collected for the selected duration of 12 months using a systematic random sampling method. For each hospital, 25 samples were taken randomly for each month of the study coverage period. Regarding prescribing indicator number 7, one hundred records were collected randomly from the medical records of community-acquired pneumonia patients from each hospital. Data for prescribing indicators 5 and 6 for patients in the obstetrics and gynecology departments were only obtained from SMC and NMC as EGH does not have such a department. One hundred records were chosen randomly from the medical archive of each hospital. Data collection methods, forms (instruments) for prescribing and patient care indicators and sample distribution for these indicators are available in (Supplementary Tables 2, 3, 6, 7).

Ethical consideration and procedures

Approval to conduct the study was obtained from Al-Azhar University followed by approval from the Directorate for Human Research- Ministry of Health-Gaza Strip. Following this approval, the Institutional Review Board of each of the study hospitals approved the study. The informed consent for this type of study was waived as data collection from patient records was done retrospectively.

Analysis of data

Statistical Package for Social Sciences SPSS version 24 and Microsoft Excel (MS Office 2010) were used for data analysis. Descriptive statistics were used to present the results. All needed computations were done using formulas stated in the WHO methodology [14] (Supplementary Table 8).

Results

Hospital indicators

Results for hospital indicators are summarized in Table 2. STGs for infectious diseases were not available except for the National surgical antibiotic prophylaxis guidelines. Despite the existence of drug and therapeutics committees (DTC) in all hospitals; none of the hospitals has its hospital formulary list.

Table 2. Hospital indicators.

Indicators	SMC	NMC	EGH	Optimal values
Indicator 1: Existence of standard treatment guidelines (STGs) for infectious diseases				
Does the hospital have standard treatment guidelines (STGs) for infectious diseases for the most prevalent conditions?	No	No	No	**Yes**
Date of last revision of the STGs for infectious diseases	N/A	N/A	N/A	
How many infectious disease treatments are listed in the STGs	1	1	1	
Indicator 2: Existence of an approved hospital essential medicines list (EML); Instrument 1				
Does the hospital have a formulary list or EML authorized for acquisition of medicines by the hospital?	No, but the hospital follows the national EML	No, but the hospital follows the national EML	No, but the hospital follows the national EML	**Yes**
Date of last revision of the formulary list or EML	2014	2014	2014	
Are all of the medicines on the formulary list identified by generic name	Yes	Yes	Yes	**Yes**
Are the formulary or EML medicines based on those recommended in the STG?	Not applicable	Not applicable	Not applicable	**Yes**
How many antibiotics are on the EML?	31	31	31	
Indicator 3: Availability of a set of key antibiotics in the hospital stores on the day of investigation				
Availability of a set of key antibiotics in the hospital stores on the day of investigation	58.6%	90.9%	44.8%	**100%**
Indicator 4: Average number of days that a set of key antibiotics is out of stock				
Average number of days that a set of key antibiotics is out of stock for the 12 months covered in the study	120.5 days	63.3 days	119.8 days	**Zero**

Table 3. The most common antibiotics that were out of stock in 2018.

Hospital	The most common antibiotics that were out of stock for the 12 months covered in the study	Total days out of stock
SMC	Cefepime injection	334
	Azithromycin tab	304
	Cephalexin cap	303
	Ampicillin injection	272
NMC	Azithromycin tab	334
	Ticoplanin injection	303
	Cefepime injection	274
	Doxycycline tab	214
EGH	Benzyl penicillin injection	306
	Azithromycin tab	303
	Cefepime injection	280
	Ampicillin 1 g + salbactam 500 mg injection	273

Table 4. Characteristics of patients in each hospital (n = 1400).

	SMC, n (%)	NMC, n (%)	EGH, n (%);	Overall
	N = 500	N = 500	N = 400	N= 1400
Gender				
Male	114 (22.8)	274 (54.8)	256 (64)	644 (46)
Female	386 (77.2)	226 (45.2)	144 (36)	756 (54)
Age (years)				
< 18	41(8.2)	55(11)	47(9.4)	143 (10.2)
18-54	369 (73.8)	280(56)	288 (57.6)	937 (66.9)
> 55	90 (18)	165(33)	65(13)	320 (22.9)
Departments				
Internal medical departments	228 (45.6)	195 (39)	215 (53.8)	638 (45.6)
Surgical departments	88 (17.6)	67 (13.4)	185 (46.2)	340 (24.3)
Gynecology and obstetrics	184 (36.8)	238 (47.6)	0 (0)	422 (30.1)

N: no. of patients; n (%): percentages are given within parenthesis with the total number of patients in each category as a denominator.

Table 5. Prescribing and patient care indicators.

Indicator	Overall	SMC	NMC	EGH	Optimal values
Prescribing indicators					
1. Percentage of hospitalizations with one or more antibiotics prescribed	68.2%	67.33%	62.6%	74.6%	20-26.8
2. Average number of antibiotics prescribed per hospitalization in which antibiotics were prescribed	1.26	1.34	1.27	1.174	1.6-1.8
3. Percentage of antibiotics prescribed consistent with the National EML	98%	100%	96%	98%	100%
4. Average duration of prescribed antibiotic treatment (days)	3	3	2.6	3.4	7-10 days
5. Percentage of patients who receive surgical antibiotic prophylaxis for Caesarean section in accordance with hospital guideline	43%	1%	85%	_	100%
6. Average number of doses of surgical antibiotic prophylaxis prescribed for Caesarean section procedures	1.9	1.8	1.9	_	1
7. Percentage of patients with pneumonia who are prescribed antimicrobials in accordance with standard treatment guidelines	6.3%	11%	3%	5%	100%
8. Percentage of antibiotics prescribed by generic name	55%	22.02%	77.17%	67.4%	100%
Patient care indicators					
1. Percentage of doses of prescribed antibiotics actually administered	97.1%	94.9%	98.2%	98.3%	
2. Average duration of hospital stay of patients who receive antibiotics (days)	4.1	4.1	3.3	4.8	

Yet, all of them follow the National essential medicine list (EML) that was approved by the Palestinian Ministry of Health in 2014. National EML includes 556 drugs listed in alphabetical order by generic names. Thirty-one antibiotics are listed in the National EML in 57 different doses and dosage forms. Key antibiotics list was obtained from the central pharmacy in each of the investigated hospitals to calculate hospital indicators 3 and 4. Key antibiotics were as follows: 29 antibiotics in SMC, 22 in NMC, and 29 in EGH. EGH reported the lowest availability of key antibiotics on the day of investigation (44.8%), and the SMC reported the highest average number of days that key antibiotics were out of stock during the year 2018 (120.5 days). The most common antibiotics that were out of stock in the three hospitals are summarized in Table 3.

Prescribing and patient care indicators

A total of 1400 patient records were screened for prescribing and patient care indicators. Characteristics of patients are summarized in Table 4 and results for prescribing and patient care indicators are summarized in Table 5. We found that 68.2% of patients were prescribed antibiotics and – on average- the duration of antibiotic treatment was 3 days. The average number of antibiotics prescribed per hospitalization was 1.26, 55% of antibiotics were prescribed by generic name and 98% were consistent with the National EML. Examples of prescribed antibiotics that were not consistent include cefepime and imipenem. Of the 781 prescribed antibiotics; 740 (94.7%) were given parenterally. Ceftriaxone was the most commonly prescribed among all antibiotics (371, 47.5) (Table 6). Only 43% of patients received surgical antibiotic prophylaxis for Caesarean section in accordance with guidelines. The average number of doses of surgical antibiotic prophylaxis was 1.9. Ceftriaxone was the most commonly prescribed antibiotic for cesarean section in SMC (76%), followed by cephalexin (23%) and cefuroxime (1%). Cefazoline was the most commonly prescribed antibiotic in NMC (82%), followed by ceftriaxone (8%), cephalexin (7%), and cefuroxime (3%). In both hospitals, the administration of prophylactic antibiotics was within 1 hour before skin incision for all patients which corresponds with guideline recommendations. The percentage of patients with pneumonia who were prescribed antibiotics in accordance with STGs was only 6.3%. Patients were treated for an average of 3.2 days. Ceftriaxone was the most commonly prescribed antibiotic (54.1%).

Regarding patient care indicators, 97% of doses of prescribed antibiotics were administered. On average, patients who receive antibiotics stayed in the hospital for 4.1 days.

Table 6. Prescribing patterns in SMC, NMC, and EGH.

	Overall (N = 781)	**SMC (N = 277)**	**NMC (N = 242)**	**EGH (N = 262)**
Number of antibiotics prescribed parenterally n (%)	740 (94.7)	254 (91.7)	227 (93.8)	259 (98.9)
Prescribed antibiotics n (%)				
Ceftriaxone	371(47.5)	141 (50.9)	107 (44.2)	123 (46.9)
Cefazolin	83 (10.6)	11 (4.3)	30 (12.4)	42 (16)
Ciprofloxacin	67 (8.6)	28 (10)	15 (6.2)	24 (9.1)
Cefuroxime	40 (5.1)	5 (1.1)	23 (9.5)	12 (4.6)
Gentamycin	29 (3.7)	21 (7.6)	7 (2.9)	1 (0.38)
Cefotaxime	24 (3.1)	15 (5.4)	7 (2.9)	2 (0.76)
Ceftazidime	23 (2.9)	7 (2.5)	7 (2.9)	9 (3.44)
Cephalexin	23 (2.9)	19 (6.8)	4 (1.65)	0 (0)
Benzylpenicillin	22 (2.8)	1(0.3)	5 (2.1)	16 (6.1)
Vancomycin	21 (2.7)	8 (2.8)	7 (2.9)	6 (2.29)
Cloxacillin	20 (2.6)	0 (0)	7 (2.9)	13 (5)
Azithromycin	19 (2.4)	12 (4.6)	7 (2.9)	0 (0)
Amikacin	13 (1.7)	2 (0.7)	6 (2.48)	5 (1.91)
Meropenem	7 (0.9)	2 (0.7)	3 (1.2)	2 (0.76)
Ampicillin	5 (0.6)	2 (0.7)	3(1.24)	0 (0)
Amoxicillin/clavulanate potassium	4 (0.5)	1(0.3)	0 (0)	3 (1.1)
Cefepime	3 (0.4)	0 (0)	2 (0.8)	1 (0.38)
Clindamycin	2 (0.3)	1(0.3)	0 (0)	1 (0.38)
Tazocin	2 (0.3)	0 (0)	0 (0)	2 (0.76)
Imipenem	1 (0.1)	0 (0)	1 (0.41)	0 (0)
Erythromycin	1 (0.1)	0 (0)	1 (0.41)	0 (0)
Doxycycline	1 (0.1)	1(0.3)	0 (0)	0 (0)

N: no. of prescribed antibiotics; n (%): percentages are given within parenthesis with the total number of prescribed antibiotics in each category as a denominator.

Discussion

Hospital indicators

Every healthcare facility should have its own formulary list (FL). It is a list of drugs that are recommended for use within the facility, and is usually developed by the DTC. Developing a hospital FL should take into consideration the best evidence, patients' needs, costs, and the STGs for treating common diseases encountered in that facility [18]. The presence of hospital formulary systems and STGs is essential to standardize therapy, and optimize patient care [14]. Besides, the availability of STGs for infectious diseases is considered an important antibiotic stewardship strategy to promote the rational use of antibiotics [19]. In the present study, the absence of FL and STGs for the most common infectious diseases was observed in all of the study settings. Thus, physicians were free to prescribe antibiotics based on their best judgment with no prescribing standards to follow. These findings are similar to those from Pakistan [9], and Eastern Ethiopia [20] where none of the assessed hospitals had developed its own STG or FL.

Optimal inpatient care would not be possible if key antibiotics are not available at all times in adequate amounts [14]. Inadequacy of key antibiotics may lead to inappropriate prescribing and poor patient outcomes [8]. Patients may be forced to purchase drugs from local pharmacies or not receive their treatment at all [9], which is a commonly observed situation. Only 58.6% and 44.8% of key antibiotics were available in SMC and EGH, respectively. The situation was better in NMC (90.9%), though not optimal. Key antibiotics were out of stock for an average of 120, 119.8, and 63.6 days/ year at SMC, EGH, and NMC, respectively. Studies from developing countries reported better results with the availability of key antibiotics ranging from 63.3%-93.8% and days out of stock ranging from 3.3 -78.18 days/year [8,9,20,21]. Our results indicate a problem in the hospital's ability to procure, distribute, or maintain a constant supply of antibiotics. This may, in part, be related to the irregularity in monthly supplies of medicines from the Palestinian Ministry of Health (MOH) due to the continuing financial crises faced by the National Palestinian Authority [22]. Indeed, a considerable percentage of the available medicines in our hospitals comes from donations rather than procurement by the MOH. Overuse of antibiotics may also have contributed to this inadequacy of antibiotics, and this is evident from the results of prescribing indicators as will be discussed later.

Prescribing indicators and prescribing patterns

In the current study, 68.2% of patients were prescribed antibiotics, which is higher than the optimal values (20-26%) suggested by previous studies [16,21]. Such overuse of antibiotics was common in Eritrea (79%) [8], Pakistan (82.3%) [9], and Yemen (84.2%) [10]. Many reasons might have contributed to this problem in our hospitals. These include a lack of written guidelines and policies to regulate antibiotic use, financial incentives from drug companies to the prescribers, and lack of continuous medical education. We also found that most antibiotics prescribed in this study (94.7%) were given parenterally. This over-prescription of injectable drugs is unacceptable due to risks of catheter-related infections, higher costs, and increased burden of nurses [23]. High rates of parenteral prescriptions of antibiotics, though lower than ours, were also observed in other studies: 82.4% in Ethiopia [24], and 81.4% in Eritrea [8].

An average of 1.26 antibiotics were prescribed per patient, which is lower than the suggested optimal values of (1.6-1.8), probably due to the poor availability of antibiotics in hospitals. Comparable results were reported by other studies, where 1.29 and 1.4 antibiotics were prescribed per patient in Eritrea [8] and Pakistan [9], respectively. Yet, considerably more antibiotics were prescribed per patient in Jordan (2.4) [25].

Antibiotics, in the present study, were prescribed for an average of 3 days which is lower than what was found in similar studies from other developing countries. In Pakistan [9] and Eritrea [8], average antibiotic treatment durations were 5.4 and 6.4 days, respectively. The 3-day antibiotic treatment duration found in our study is generally short compared to the recommendations of 7-10 days of treatment. This may prolong hospital stay and promote AMR [14]. Further analysis of medical records revealed that some patients were discharged on their own responsibility before they had completed the antibiotic course. Patients may prefer completing their treatment at home due to the crowdedness in hospital wards, especially if their health permits. We also found that for some patients antibiotics were changed shortly after the initiation of treatment. We didn't, however, investigate the reasons behind this. This may be rational if changes were done for clinical reasons, such as switching to narrower spectrum antibiotics following culture sensitivity results, switching to oral alternatives after the patient's condition has been stabilized, or changing an antibiotic due to intolerable or serious adverse effects. Yet, switching to another antibiotic before completing a course of treatment may be due to stock shortages and

the inability of the patient to purchase the initially recommended antibiotic. This assumption is in line with our findings of the poor availability of key antibiotics in the investigated hospital stores.

The current study reveals considerably low adherence rates to the national STG for Caesarean section antibiotic prophylaxis (43% overall, 1% in SMC, and 85% in NMC). The very low adherence rate in SMC was due to choosing ceftriaxone instead of the recommended cefazolin and it was comparable to those from Pakistan (0%) [9] and India (5.6%) [26]. Since there were no national or hospital STGs for pneumonia in the three hospitals, the American Thoracic Society and Infectious Diseases Society of America (DTS/ IDSA) guidelines [27] were used to assess pneumonia treatment practice. We found a very low adherence rate to the guidelines (6.3%). Meanwhile, studies from other developing countries found the following adherence rates to pneumonia guidelines: 0% in Pakistan [9], 25% in Ghana [28], and 35.4% in Ethiopia [29]. The extremely low adherence to pneumonia guidelines in our study may be explained by the lack of awareness of the STGs by some physicians and the absence of institutional or even national STGs. In addition, some of the recommended antibiotics by guidelines such as ampicillin + sulbactam and azithromycin were frequently out of stock while others are not listed in the National EML such as ceftaroline, clarithromycin, levofloxacin, and moxifloxacin and are unavailable in hospital stores.

We found that only 55% of antibiotics were prescribed by generic name with the percentage in SMC as low as 22%. This is much lower than findings from other studies where generic prescribing rates ranged from 71.6 to 98.4% [8, 15,21]. Low rates of generic prescriptions in our hospitals can be explained by the familiarity of physicians with brand names and the absence of policies regulating prescription writing. Generic prescribing should be encouraged as it leads to better communication among healthcare providers [14], decreases confusion over drug terminology that can lead to prescribing errors, and supports efforts to minimize the commercial influence on medical practice [30].

Patient's related indicators

The average duration of hospital stay of patients who receive antibiotics was 4.1 days. This is lower than the average of 9.9 days reported in Eritrea [15], or 6.4 days reported in Pakistan [9]. We found that 97.1% of doses of prescribed antibiotics were actually administered to patients. This is an acceptable value (close to the optimal 100%) and may reflect good medication administration practice by nurses. Yet, our results should be interpreted with caution. In our study, the administration of antibiotic doses was evaluated by reviewing patients' records. However, this method of evaluation is not accurate compared to the direct observation method and can lead to an overestimation of results.

Strengths and limitations

Finally, it is worth mentioning the strengths and weaknesses of this study. This study is the first to investigate antibiotic use in Palestinian hospitals using WHO indicators. Yet, there are some limitations in our study that need to be clarified. First, this study was conducted in governmental hospitals in the Gaza Strip, therefore generalization of our results to other governmental hospitals in Palestine or nongovernmental hospitals in the Gaza strip cannot be justified. Second, regarding prescribing indicators, this study assessed only inpatient departments and cannot reflect outpatient prescribing patterns or care.

Conclusions

Antibiotics utilization is less than optimal in Gaza Strip hospitals. This is in terms of STGs availability, adherence to STGs for cesarean section antibiotic prophylaxis and those for CAP treatment, antibiotic stock out days, percentage of antibiotics prescribed, and generic prescribing. The MOH should fill the gaps in the availability and affordability of medicines, including antibiotics. DTCs should be activated to develop and regularly update hospital formulary lists, STGs for infectious diseases as well as drug-related policies to regulate antibiotic use and prescribing in hospitals. Continuous education and training programs for healthcare practitioners regarding the rational use of antibiotics should be implemented and their impact on antibiotic use should be assessed.

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Annex – Supplementary Items

Supplementary Table 1. Data collection methods and instruments for hospital indicators.

Indicator	Data collection method	Participants	Instrument number /question number
Existence of standard treatment guidelines (STGs) for infectious diseases	Interview	Pharmacy director	Instrument 1, questions 8,9 and 10
Existence of an approved hospital formulary list or essential medicines list (EML)	Interview	Pharmacy director	Instrument 1, questions 3, 4,5,6 and 7
Availability of a set of key antibiotics in the hospital stores on the day of the study	Review of inventory records	Pharmacy director	Instrument 2
Average number of days that a set of key antibiotics is out of stock	Review of inventory records	Pharmacy director	Instrument 2

Supplementary Table 2. Data collection methods for prescribing and patient care indicators.

Indicator	Data collection method	Participants	
Prescribing indicators			
1. Percentage of hospitalizations with one or more antibiotics prescribed	Patients' charts review	Patients from all hospital departments	Instrument 3
2. Average number of antibiotics prescribed per hospitalization in which antibiotics were prescribed	Patients' charts review	Patients from all hospital departments	Instrument 3
3. Percentage of antibiotics prescribed in consistency with the hospital formulary list	Patients' charts review	Patients from all hospital departments	Instrument 3
4. Average duration of prescribed antibiotic treatment	Patients' charts review	Patients from all hospital departments	Instrument 3
5. Percentage of patients who receive surgical antibiotic prophylaxis for cesarean section in accordance with hospital guideline	Patients' charts review	Patients from gynecology and obstetrics department	Instrument 4
6. Average number of doses of surgical antibiotic prophylaxis prescribed for cesarean section procedures	Patients' charts review	Patients from gynecology and obstetrics department	Instrument 4
7. Percentage of patients with pneumonia who are prescribed antibiotics in accordance with standard treatment guidelines	Patients' charts review	Patients from respiratory department	Instrument 3
8. Percentage of antibiotics prescribed by generic name	Patients' charts review	Patients from all hospital departments	Instrument 3
Patient care indicators			
1.Percentage of doses of prescribed antibiotics actually administered	Patients' charts review	Patients from all hospital departments	Instrument 3
2. Average duration of hospital stay of patients who receive antibiotics	Patients' charts review	Patients from all hospital departments	Instrument 3

Supplementary Table 3. Sample Distribution for prescribing and patient care indicators (n = 1400).

Hospital	Number of records	Department
Al Shifa Medical Complex (SMC)	300 records	All hospital departments
	100 records	Gynecology and obstetrics
	100 records	Respiratory department
Nasser medical complex (NMC)	300 records	All hospital departments
	100 records	Gynecology and obstetrics
	100 records	Respiratory department
European Gaza hospital (EGH)	300 records	All hospital departments
	100 records	Respiratory department
Total	**1400 records**	

Supplementary Table 4. Instrument 1.

Name of unit:	**Data collector:**	**Date:**

1. Does the hospital have a Drug and Therapeutics Committee?
2. If affirmative, when was the last meeting? [Review the minutes.]
3. Does the hospital have a formulary list or EML authorized for acquisition of medicines by the hospital
4. Date of last revision of the formulary list or EML?
5. If yes, how many antibiotics are on the formulary list or EML? [Request a copy of the list.]
6. Are all of the medicines on the formulary list identified by generic name (INN)?
7. Are the formulary or EML medicines based on those recommended in the STG?
8. Does the hospital have standard treatment guidelines (STGs) for infectious diseases for the most prevalent conditions? _____ For pneumonia? _____ [Request a copy.]
9. Date of last revision of the STGs for infectious diseases?
10. How many infectious disease treatments are listed in the STGs?
11. Does the hospital laboratory routinely perform antibiotic drug sensitivity tests (antibi grams, cultures)?
12. How many discharges did the hospital have during the last calendar year?
13. How many surgical interventions were performed during the last calendar year?
14. Does the hospital have protocols or norms for surgical prophylaxis with antibiotics?

Supplementary Table 5. Instrument 2: Availability of a set of key antimicrobials and time out of stock.

Name of unit:														
Data collector:														
Date:														
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Product (Generic name, form, and strength)	Current stock	Days Out of Stock												
		M1 Last month	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	Total days out of stock
														Total:

Supplementary Table 6. Instrument 3: Form to record antibiotics.

Name of unit:													
Data collector:													
Date:													
Patient information				Antimicrobial information									
1	2	3	4	5	6	7	8	9	10	11	12	13	14
Clinical history No.	Pneumonia case/ (Y/N)	Was antibiotic prescribed? (Y/N)	No. of days in hospital	Was sensitivity test done? (Y/N)	Name(s) of antibiotic(s) prescribed	INN used? (Y/N)	Antibiotic on FL? (Y/N)	Dosage form and strength	Total days of treatment	No. of antibiotics of same generic type prescribed	Dosage frequency/d	Doses prescribed	Doses administered
Total cases	Total (Ys)	Total (Ys)	Total days	Total (Ys)	Total	Total (Ys)	Total (Ys)	-	Total days	Total generic	-	Total doses	Total doses

Supplementary Table 7. Instrument 4: Form to record Cesarean Section surgical prophylaxis.

Name of unit:					
Data collector:					
Date:					
1	2	3	4	5	6
CH No.	Surgical procedure	Prophylaxis (Y/N)	Surgical antibiotic prophylaxis for Cesarean Section in accordance with hospital guidelines (Y/N)	Antibiotic prescribed (name, dosage form and strength)	Number of doses

Supplementary Table 8. Formulas to calculate quantitative indicators.

Indicator	Calculation
Hospital indicators	
3.Availability of a set of key antibiotics in the hospital stores on the day of the study	$\frac{Number\ of\ key\ antibiotics\ actually\ in\ stock}{Number\ of\ key\ antibiotics\ that\ should\ be\ available} \times 100$ The necessary information found on Instrument 2, and is calculated by adding the total numbers of entries in column 2 (current stock) that are more than 0 and then dividing by the total number of products in column 1.
4.Average number of days that a set of key antibiotics is out of stock	$\frac{Number\ of\ days\ that\ each\ antibiotic\ is\ out\ of\ stock}{Number\ of\ key\ antibiotics\ in\ the\ review} \times 100$ The information is found on Instrument 2, and is calculated by adding the total days out of stock in column 15, then dividing by the number of products in column 1.
Prescribing indicators	
1.Percentage of hospitalizations with one or more antibiotics prescribed	$\frac{Number\ of\ patient\ hospitalizations\ with\ one\ or\ more\ antibiotics\ prescribed}{Total\ number\ of\ hospitalizations\ studied} \times 100$ The information is found on Instrument 3 and is calculated by adding the total of Ys in column 3, dividing by the total number of patients in column 1, and multiplying by 100.
2.Average number of antimicrobials prescribed per hospitalization in which antibiotics were prescribed	$\frac{Number\ of\ antibiotics\ prescribed\ for\ all\ hospitalizations}{Total\ number\ of\ hospitalizations\ with\ antibiotics\ prescribed}$ The information is found on Instrument 3, and is calculated by dividing the total in column 11 by the total Ys of column 3.
3.Percentage of antibiotics prescribed consistent with the hospital formulary list	$\frac{Number\ of\ antibiotics\ prescribed\ that\ are\ on\ the\ formulary\ list}{Number\ of\ antibiotics\ prescribed} \times 100$ The information is found on Instrument 3, and is calculated by adding the number of Ys in column 8, dividing by the total of column 6, and multiplying by 100.
4.Average duration of prescribed antibiotic treatment	$\frac{Total\ number\ of\ days\ on\ antibiotic\ treatment}{Total\ number\ of\ antibiotics\ prescribed}$ The information is found on Instrument 3, and is calculated by dividing the total number of days in column 10 by the total number of generic antimicrobials of column 11.
5.Percentage of patients who receive surgical antibiotic prophylaxis for cesarean section in accordance with hospital guideline*	$\frac{Percentage\ of\ patients\ receiving\ surgical\ antibiotic\ prophylaxis\ for\ cesarean\ section\ in\ accordance\ with\ hospital\ guidelines}{Total\ number\ of\ patients\ with\ cesarean\ section\ procedures} \times 100$ The information is found on Instrument 4, and is calculated by adding the total Ys of column 4, dividing by the total number of cesarean section procedures listed in column 2, and multiplying by 100
6.Average number of doses of surgical antibiotic prophylaxis prescribed for cesarean section procedures	$\frac{Number\ of\ doses\ of\ surgical\ antibiotic\ prophylaxis\ for\ cesarean\ section}{Total\ number\ of\ cesarean\ section\ procedures}$ The information is found on Instrument 4, and is calculated by adding the total number of doses in column 5, then dividing by the total number of Ys for prophylaxis in column 3.
7.Percentage of patients with pneumonia who are prescribed antibiotics in accordance with standard treatment guidelines**	The compliance of prescribers with hospital treatment standards is defined by (a) use of only antibiotics of choice as defined in the STG, and (b) observance of dosing indications for the same antibiotics **The percentage for (a):** $\frac{Number\ of\ pneumonia\ patients\ treated\ only\ with\ antibiotics\ per\ STG}{Total\ number\ of\ patients\ with\ pneumonia} \times 100$ **The percentage for (b):**

	$\frac{\frac{Number\ of\ pneumonia\ patients}{prescribed\ correct\ dose\ of\ correct\ antibiotic\ per\ STG}}{\frac{Number\ of\ pneumonia\ patients}{who\ received\ the\ recommended\ antibiotic\ per\ STG}} \times 100$ The information is found on Instrument 3 and is calculated by looking at each treatment for pneumonia shown by a Y in column 2 and comparing it with the STG.
8.Percentage of antibiotics prescribed by generic name	$\frac{Total\ number\ of\ antibiotics\ prescribed\ by\ generic\ name}{Total\ number\ of\ doses\ of\ antibiotics\ prescribed} \times 100$ The information is found on Instrument 3. The percentage is calculated by dividing the total Ys of column 7 by the total of column 6 and multiplying by 100.
Patient care indicators	
1.Percentage of doses of prescribed antibiotics actually administered	$\frac{Number\ of\ doses\ of\ antibiotics\ administered}{Total\ number\ of\ doses\ of\ antibiotics\ prescribed} \times 100$ The information is found on Instrument 3, and is calculated by dividing the total doses administered in column 14 by the total doses prescribed in column 13 and multiplying by 100.
2.Average duration of hospital stay of patients who receive antibiotics	$\frac{Total\ number\ of\ days\ of\ hospitalization\ for\ patients\ receiving\ antibiotics}{Number\ of\ patients\ receiving\ antibiotics}$ The information is found on Instrument 3, and is calculated by finding the total days in hospital of column 4 and dividing by the total Ys in column 3.

* = Palestinian Ministry of Health guidelines; ** = Official Clinical Practice Guidelines of the American Society and Infectious Diseases Society of America.