Antimicrobial resistance patterns of Acinetobacter baumannii colonization patient's skin.

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Abstract:

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Background: Acinetobacter baumannii is a significant opportunistic pathogen and it is generally associated with benign colonization of hospitalized patients.

Objective: To investigate skin colonization with Acinetobacter baumannii in hospitalized patients and healthy volunteers. Antimicrobial resistance patterns of Acinetobacter baumannii was assessed by determining the minimum inhibitory concentrations (MICs) of thirteen different antimicrobial agents. Accepted: April. 2020

Patients and Methods: The study performed on hospitalized patients at Rizgary and Hawler teaching hospitals and healthy volunteers who attended to supermarkets in Erbil, Iraq. A single sample was obtained once from each of the forehead, one ear pinna, one armpit, finger webs of one hand and toe webs of one foot to isolated Acinetobacter baumannii, then identified using phenotypic and genotypic properties. All isolates examined for their antimicrobial susceptibility by the agar dilution method.

Results: Among 600 hospitalized patients, 79 (13.17%) colonized with Acinetobacter baumannii, yielding 155 isolates that are resistant to 57.42% ceftriaxone, 56.77% cefotaxime, 45.81% ceftazidime and 40.65% ciprofloxacin. While the most effective antimicrobial agents with MIC_{50/90} values (minimum inhibitory concentrations required to inhibit 50% and 90% of the isolates, respectively) were as follows: imipenem, 80.65%, 0.25/16 mg/L; doxycycline, 80.65%, 1/16 mg/L; amikacin, 79.35%, 2/64 mg/L. However, 53 Acinetobacter baumannii isolated from healthy volunteers that showed resistance to 50.94% ceftriaxone (MIC_{50/90}, 64/128 mg/L), 45.28% ceftazidime, 43.40% cefotaxime, and 35.85% ciprofloxacin. Fortunately, all 208 Acinetobacter baumannii were sensitive to polymyxin B (MIC₅₀=0.25mg/L).

Conclusion: The rates of Acinetobacter baumannii colonized patients higher than healthy volunteers, whereas an antimicrobial minimum inhibitory concentrations value of cefepime, cefotaxime, imipenem, amikacin, ciprofloxacin, and levofloxacin were significantly higher in patients than healthy volunteers. Polymyxin B had activity against all Acinetobacter baumannii strains.

Keywords: Antibiotic resistance; Colonization; Multidrug resistance; MIC values.

Introduction:

Acinetobacter baumannii (A. baumannii) is a Gramnegative, non-fermenting coccobacilli bacteria and it is an important opportunistic pathogen involved in several types of infection with high mortality and morbidity(1). A. baumannii can form part of the endogenous bacterial skin flora and the humidity is a common environmental factor associated with skin colonization (2). A. baumannii has a reservoir in the non-hospitalized individuals, from which the bacteria can be introduced into a hospital (3). Indications that the skin colonized is an important source of infections in hospitalized patients, thereby contributing to the involved in the nosocomial infections and hospital outbreaks (4). As well, a high colonization rate of body sites has been documented in outbreaks (5), when the patient admitted to the same hospital ward, these bacteria may be transmitted and new patients colonized and acquiring A. baumannii (6). The incidence of A. baumannii infections varies widely, from less than 1% to 32% (7, 8).

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Besides, it's easily acquired resistance to different and multiple classes of antimicrobial and their ability to become resistant to almost all antimicrobial agents, lead to rapid developing multidrug-resistant A. baumannii (9). This can effect on any antimicrobial drugs used in clinical practice. Hence, in A. baumannii infections, several drugs and drug classes were definitively eliminated from treatment strategy (10). The ability of A. baumannii to colonize patients and its resistance phenotype makes prevention and control of outbreaks caused by this bacteria difficult (11), which reported that the prevalence of A. baumannii infections and resistance to antimicrobial agents have been increased steadily (12). Besides that, the emergence of multiantimicrobial resistant among A. baumannii strains been described worldwide have as (13).Unfortunately, A. baumannii is one of the most bacterial resistance in the clinical practice, and making the process of therapy is a challenge (14). This prompted several microbiological studies antimicrobial resistance in Α. baumannii. Antimicrobial resistance greatly limits the treatment options for patients who are infected with this bacteria, especially if isolates are multidrug-resistant (15). However, slight is known about the natural reservoirs of *A. baumannii*. To further assess the natural habitats, the current study investigated the frequency and distribution of *A. baumannii* on various body sites among patients and healthy volunteers, then determined their antimicrobial susceptibility by minimum inhibitory concentration (MIC).

Patients and Methods:

Skin swabs were collected from hospitalized patients and healthy volunteers from July 2015 to January 2019. The patient group consisted of 600 patients who hospitalized for various diseases in a regular ward at Rizgary and Hawler teaching hospitals with 493 and 500 beds, respectively located in Erbil Governorate, Iraq. The healthy volunteer group included 900 non-hospitalized individuals who attended to Erbil supermarkets as a community population.

The exclusion criteria in both patients and healthy volunteer groups were included the following: age <18 years, refusal to participate, pregnancy, antibiotic use in the previous week, or any surgery within the prior 4 weeks. Verbal informed consent was taken from the participant before being enrolled in this study.

Sample Collection: A sterile moistened swab was rubbed vigorously, with rotation, over areas 6-12 cm² of 5 different body sites of forehead, one ear pinna, one armpit, finger webs of one hand and toe webs of one foot (16, 17), yielded 75,000 swabs of 600 hospitalized patients and 900 healthy volunteer's.

Identification of Acinetobacter baumannii: All swabs taken were streaked onto the Blood agar supplemented with 4 μ g/ml vancomycin (Sigma-Aldrich), MacConkey agar and CHROMagar Acinetobacter (CHROMagar, Paris, France) plates then cultured at 35°C for 48 h(18).

The bacteria identified presumptively as *Acinetobacter* species by standard laboratory methods (19). Then the isolates consistently identified *A. baumannii* with the API 20 NE system(bioMérieux, France) according to the manufacturer's instructions.

The PCR protocol was used to confirm the *A*. *baumannii* by amplify the gene encoding *bla*OXA-51-like. Primary PCR was run using forward primer 5'-TAA TGC TTT GAT CGG CCT TG-3'and reverse primer 5'-TGG ATT GCA CTT CAT CTT GG-3' to amplify a 353 bp fragment (20).The isolated bacteria not confirmed by PCR were excluded from the study.

The distinct body sites colonized with *A. baumannii* is shown in Table 2, so that 40.51% patients and

Antimicrobial susceptibility testing: The MIC testing of antimicrobial agents was performed by agar dilution technique according to the Clinical Laboratory Standard Institute (CLSI) guideline (21)*A. baumannii* tested against ceftazidime, cefepime, cefotaxime, ceftriaxone, imipenem, meropenem, polymyxin B, gentamicin, tobramycin, amikacin, doxycycline, ciprofloxacin and levofloxacin (Sigma-Aldrich). The MICs interpreted according to CLSI criteria and its susceptibility determined based on CLSI breakpoints(22).

Statistical analysis:

Data were recorded using Microsoft Excel, and all statistical analyses performed using SPSS software 25 for Windows. Percentage, range, and mean \pm standard deviation (SD) were used to describe and analyze the data. The differences between categorical variables were analyzed by the Pearson Chi-Square test. T test used to assess the statistical significance between antimicrobial MIC of *A*. *baumannii* colonized patients and healthy volunteers. All tests were two-sided, with a *P* value of ≤ 0.05 is significant.

Results:

During three years and six months of the study period, 7,500 skin swabs were collected from 600 patients and 900 healthy volunteers in order that five swabs were obtained from each individual, so that yielded 208*A*. *baumannii* isolates. The isolated bacteria were recovered from 79 patients (155 isolates) and 33 healthy volunteers (53 isolates) as a result give colonized rate13.17% in patients and 3.67% of healthy volunteers, thus the distribution of the isolates was significantly higher in the patient group than the healthy volunteers (P=0.022) (Table 1).

 Table 1: Distribution of A. baumannii colonized

 patient and healthy volunteer groups

Colonization	Patient		Healthy volunte	y eers	Both groups			
characteristic	n	%	Ν	%	n	%		
Skin colonized	79	13.17	33	3.67	112	7.47		
Non- colonized	521	86.83	867	96.33	1388	92.53		
Total no.	600		900		1500			
No. of <i>A.</i> baumannii	155		53		208			

(P=0.022, Pearson Chi-Square).

27.27% healthy volunteers were colonized with *A. baumannii* at two different body sites. In addition, the bacteria were isolated from three different body sites in 17.72% patients and 12.12% healthy volunteers. Instead 35.44% patients and 57.58% healthy volunteers colonized one body site. Furthermore, there was a significant difference

between patients and healthy volunteer group (P=0.024).

	Patients group	р		Healthy volunteers' group				Both groups			
<i>n</i> of colonization in body sites	<i>n</i> of patients	%	n of A.baumannii	<i>n</i> of volunteers	of volunteers %		п	%	n of A. baumannii		
One body site	28	35.44	28	19	57.58	23	47	41.96	51		
Two body sites	32	40.51	64	9	27.27	18	41	36.61	82		
Three body sites	14	17.72	42	4	12.12	8	18	16.07	50		
Four body sites	4	5.06	16	1	3.03	4	5	4.46	20		
Five body sites	1	1.27	5	0	0.00	0	1	0.89	5		
Total	79		155	33		53	112		208		

(P=0.024, Pearson Chi-Square).

A total of 208 *A. baumannii* colonized body sites in patients and healthy volunteers, the higher percentage were colonized webs (28.85%), followed by the armpit (24.52%), finger webs (19.71%),

ear pinna (15.38%), and the forehead (11.54%). There was no significant difference between colonization body sites of patients and healthy volunteers (Table 3).

Table 3: Rates of A. baumannii colonized on forehead	, ear pinna, armpit, finger webs and toe webs.
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Skin colonized	Patients ($n = 79$)		Healthy volunteers (n.	=33)	Both groups ($n = 112$)		
	n of A. baumannii	%	n of A. baumannii	%	n of A. baumannii	%	
Forehead	18	11.61	6	11.32	24	11.54	
Ear pinna	24	15.48	8	15.09	32	15.38	
Armpit	38	24.52	13	24.53	51	24.52	
Finger webs	31	20.00	10	18.87	41	19.71	
Toe webs	44	28.39	16	30.19	60	28.85	
Total no. of isolates	155		53		208		

No significant difference association between groups (P=0.998, Pearson Chi-Square).

In patient group, the most antimicrobial effects against *A. baumannii* were polymyxin B (100%), followed by imipenem (80.65%), doxycycline (80.65%), amikacin (79.35%), levofloxacin (78.71%) meropenem (78.06%) and tobramycin (74.19%). Furthermore, The MIC₉₀ value of ceftazidime, cefotaxime and ceftriaxone were 128 mg/L. Otherwise polymyxin B has the lowest MIC_{50/90} values (0.25/0.5 mg/L) with MIC range between ≤ 0.06 to 2 mg/L. All results of antimicrobial susceptibility test and the MIC values are summarized in the Table 4.

Among healthy volunteer group, all *A. baumannii* was sensitive to polymyxin B. Besides that, the MIC range of polymyxin B was $\leq 0.06-1$ mg/L, and MIC_{50/90} value was 0.25/1 mg/L. Instead, the MIC value of ceftriaxone was highest (128 mg/L). The distributions of MIC values and the antimicrobial susceptibility are listed in Table 5.

The mean of antimicrobial MIC±SD values for the entire set of *A. baumannii* isolates from patients and healthy volunteers are shown in Table 6. Statistically, the MIC values of cefepime, cefotaxime, imipenem, amikacin, ciprofloxacin and levofloxacin higher in the patients than healthy volunteer group

Table 4: Distributions of MIC MICso and MICso values of 1554 haumannii colonized nat	tionts
Table 4. Distributions of MIC, MICs and MICs values of 155A. Daumanna colonized par	nemis.

Antimicrobial	Rates	tates of isolates with MIC, mg/L													MIC, mg/L			Susceptibility rates		
agent	≤0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	≥128	MIC ₅₀	MIC ₉₀	Range	S	Ι	R		
Ceftazidime				1.29	12.26	9.03	15.48	10.97	5.16	15.48	18.06	12.26	16	128	0.5- ≥128	49.03	5.16	45.81		
Cefepime				0.65	15.48	10.97	12.26	18.71	5.81	9.68	18.06	8.39	8	64	0.5- ≥128	58.06	5.81	36.13		
Cefotaxime				0.65	4.52	10.32	7.10	5.81	7.10	7.74	30.32	26.45	64	128	0.5- ≥128	28.39	14.84	56.77		
Ceftriaxone				1.29	4.52	9.68	7.74	5.16	5.81	8.39	40.65	16.77	64	128	0.5- ≥128	28.39	14.19	57.42		
Imipenem	15.48	21.29	20.00	13.55	7.10	3.23	0.65	4.52	7.10	5.81	1.29		0.25	16	≤0.06- 64	80.65	0.65	18.71		
Meropenem		5.16	38.06	23.23	6.45	5.16	3.87	12.90	4.52		0.65		0.5	8	0.13- 64	78.06	3.87	18.06		
Polymyxin B	14.19	20.00	45.81	17.42	1.94	0.65							0.25	0.5	≤0.06- 2	100.00	0.00	0.00		
Gentamicin			1.94	5.16	35.48	11.61	3.87	2.58	17.42	11.61	10.32		2	64	0.25- 64	58.06	2.58	39.35		
Tobramycin			23.23	29.68	17.42	3.87	1.94	12.90	7.10	3.87			0.5	16	0.25- 32	74.19	1.94	23.87		
Amikacin		1.94	14.19	13.55	10.97	15.48	12.26	7.10	3.87	3.23	12.26	5.16	2	64	0.13- ≥128	79.35	3.23	17.42		
Doxycycline	4.52	5.81	8.39	15.48	21.29	12.90	12.26	1.94	11.61	5.16	0.65	•	1	16	≤0.06- 64	80.65	1.94	17.42		
Ciprofloxacin	6.45	10.97	12.26	23.23	5.81	0.65	3.87	7.74	9.68	10.97	8.39		0.5	32	≤0.06- 64	58.71	0.65	40.65		
Levofloxacin		8.39	7.74	36.77	14.19	11.61	1.29	4.52	5.81	9.03	0.65		0.5	32	0.13- 64	78.71	1.29	20.00		

I = intermediate; MIC = minimum inhibitory concentration; $MIC_{50} = MIC$ for 50% of the isolates; $MIC_{90} = MIC$ for 90% of the isolates; R = resistant; S = susceptible.

Table 5: Distributions of MIC, MIC ₅₀ and MIC ₉₀ values of 53 A. baumanniicolonized healthy volunt	eers
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Antimicrobial	Rates of isolates with MIC, mg/L											MIC, mg/L			Susceptibility rates			
agent	≤0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	≥128	MIC ₅₀	MIC ₉₀	Range	S	Ι	R
Ceftazidime				1.89	7.55	7.55	16.98	11.32	9.43	20.75	22.64	1.89	16	64	0.5-≥128	45.28	9.43	45.28
Cefepime			5.66	22.64	20.75	13.21	3.77	1.89	3.77	13.21	15.09		2	64	0.25-64	67.92	3.77	28.30
Cefotaxime			1.89	5.66	9.43	13.21	7.55	7.55	5.66	5.66	33.96	9.43	16	64	0.25-≥128	45.28	11.32	43.40
Ceftriaxone					1.89	9.43	9.43	7.55	9.43	11.32	18.87	32.08	64	128	1-≥128	28.30	20.75	50.94
Imipenem		5.66	35.85	39.62	5.66	1.89	1.89	9.43		-			0.5	4	0.13-8	88.68	1.89	9.43
Meropenem		5.66	32.08	33.96	15.09	1.89		11.32					0.5	8	0.13-8	88.68	0.00	11.32
Polymyxin B	13.21	26.42	33.96	16.98	9.43								0.25	1	≤0.06-0.5	100.00	0.00	0.00
Gentamicin			0.13	0.25	0.11	0.11	0.06	0.02	0.13	0.15	0.04		2	32	≤0.06-64	66.04	1.89	32.08
Tobramycin		3.77	28.30	30.19	13.21	1.89		13.21	7.55	1.89			0.5	8	0.13-32	77.36	0.00	22.64
Amikacin		1.89	5.66	30.19	28.30	16.98	7.55	3.77	1.89		3.77		1	4	0.13-64	96.23	0.00	3.77
Doxycycline	1.89	5.66	26.42	32.08	11.32	5.66	1.89	3.77	5.66	3.77	1.89		0.5	16	≤0.06-64	84.91	3.77	11.32
Ciprofloxacin		1.89	28.30	24.53	7.55	1.89	13.21	15.09	3.77	1.89	1.89		0.5	8	0.13-64	62.26	1.89	35.85
Levofloxacin		1.89	26.42	39.62	13.21	5.66		9.43	3.77				0.5	8	0.13-16	86.79	0.00	13.21

I = intermediate; MIC = minimum inhibitory concentration; $MIC_{50} = MIC$ for 50% of the isolates; $MIC_{90} = MIC$ for 90% of the isolates; R = resistant; S = susceptible.

	Mean±SD of MIC, m	P		
Antimicrobial agent	Patients	Healthy volunteers	Both groups	value
Ceftazidime	34.84±41.56	26.88±27.85	32.81±38.63	0.196
Cefepime	28.69±37.80	15.39±23.22	25.30±35.10	0.017
Cefotaxime	57.88±48.41	37.83±40.19	52.77±47.18	0.007
Ceftriaxone	52.06±42.66	59.45±51.88	53.95±45.17	0.305
Imipenem	4.50±10.69	1.22±2.28	3.66±9.40	0.028
Meropenem	2.71±6.34	1.35±2.42	2.36±5.63	0.130
Polymyxin B	0.27±0.22	0.31±0.27	0.28±0.23	0.308
Gentamicin	14.09±19.84	10.23±15.67	13.11±18.90	0.200
Tobramycin	3.94±7.18	3.26±6.12	3.77±6.92	0.540
Amikacin	17.69±33.05	4.11±12.25	14.23±29.76	0.004
Doxycycline	5.15±9.33	4.16±10.89	4.90±9.73	0.525
Ciprofloxacin	11.44±18.92	4.46±10.01	9.66±17.34	0.011
Levofloxacin	5.23±10.53	1.87±3.59	4.38±9.38	0.024

Table 6: Compared antimicrobial MICs values of A. baumannii colonized patients with healthy volunteers

Discussion:

The study investigated the distribution and prevalence of A. baumannii colonized the hospitalized patient and healthy volunteers. Although it is largely accepted that the A. baumannii is colonize the human skin (23). A few studies have specifically addressed the colonization of human skin with A. baumannii. The present study focused on antimicrobial resistance, which is one of the most problematic worldwide by determining antimicrobial susceptibilities of A. baumannii recovered from patients and healthy volunteers. Interestingly, in the current study, the rate of colonized with A. baumannii was 3.59 times greater in patients than healthy volunteer groups. This probably due to the warm, moist atmosphere in the patient beds and most patients may be shower and bathe less frequently than healthy volunteers (24). Suggesting that a hospital environment becomes endemic colonization by A. baumannii. Furthermore the most important cause of this intermittent outbreak was an admission of colonized patients to the hospital and consequently spread of A. baumannii to other patients (25), which is supported that the skin colonization with A. baumannii might serves as a source of the infections. In another study, a high percentage of patients(60%) were colonized with A. baumannii (26) in comparison with the present study. In the former study, A. baumannii- A. calcoaceticus colonized 17% healthy soldiers returning from Afghanistan and Iraq (27). This proportion may be due to the endemic outbreak. Two attributes were involved in the significant of A. baumannii as a human pathogen; First, its capability to colonize and survive for a long time with a risk of an endemic spread (28).Patients who are colonize multiple body sites, and its ease of spread between patients have led to an important role the infections (29, 30). In order that the patients

colonized at different body sites is assumed to have the same strain at each site. Second, its resistance to several antimicrobial agents that complicates the treatment of the infections (31). A requirement for the improvement of new drugs against A. baumannii because an outbreaks of multidrug resistant A. baumannii have been reported in worldwide (32). The SENTRY antimicrobial surveillance program reported that the incidence of polymyxin B resistance ranging from 1.7% in Latin North America to 1.9% in the Asia-Pacific region, 2.7% in Europe (33), and 18.1% in Korea (34). Fortunately, all A. baumannii isolates in current study remain sensitive to polymyxin B as for MIC₅₀ and MIC₉₀ are lower than other studies (33, 34). Therefore, polymyxin B used as the last line therapy (35). In a study of New York City hospitals, 69% of *A. baumannii* were resistant to meropenem (36), which is highly resistance than this study, but lower resistance (8.3%) in Korea (34). The resistance rate to imipenem in this study was lower than that conducted in Lebanon, showing that the resistance to imipenem was 78% (37) and 11.7% in Korea (34). The present study reported that doxycycline has activity against A. baumannii, its slightly similar to other studies in the USA, up to 90% of the bacteria were reported as susceptible to doxycycline compared with only32% in Spain (38). The differences in antimicrobial resistance have been observed between countries, between infection and colonization, as well as between hospitalized patients and healthy volunteers as in the current study. These differences may reflect differential epidemiological situations and difference of antibiotic use between countries (30). Colonization individuals have been contributed factor to the increase and spread of the antimicrobial resistant to the environment (39). Moreover, the differences in resistance patterns among isolates underline the significance of

surveillance in determining the most sufficient therapy for *A. baumannii* infections (40).

Conclusions:

The colonization rates of *A. baumannii* strains in patients were nearly four times higher than healthy volunteers, and the antimicrobial MIC values of the most isolates were higher in patients than in healthy volunteers. The resistant strains are quite an alarming public health problem. But, polymyxin B has been the most effective antimicrobial agent against all *A. baumannii* strains.

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أنماط مقاومة Acinetobacter baumannii للمضادات الحيوية المستعمرة لبشرة المرض

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الخلاصة

الخلفية: المستشفيات من استعمار المستمفيات (ي هام يرتبط بشكل عام على استعمار المرضى في المستشفيات. الهدف: الإستقصاء عن استعمار (MICs) للمتعافر (MICs) للجلد في مرضى المستشفيات والمتطوعين الأصحاء ثم تقييم أنماط مقاومتها للمضادات الحيوية من خلال تحديد قيم التركيز المثبط/*لأدنى*(MICs) لثلاثة عشر مضاد حيوي. طريقة البحث: أجريت الدراسة على المرضى في المستشفيات رزكاري و هولير التعليمية وكذالك على المتطوعين الأصحاء الذين حضر وا إلى محلات محلوية. السوبر ماركت في أربيل ، العراق. أخذ عينة واحدة من الجبهة ، صنار أذن ، إبط ، أصابع يد و أصابع قدم لعزول الأصحاء الذين حضر وا إلى محلات السوبر ماركت في أربيل ، العراق. أخذ عينة واحدة من الجبهة ، صنار أذن ، إبط ، أصابع يد و أصابع قدم لعزول الأصحاء الذين حضر وا إلى محلات من محلات المظهرية والأنماط الور اثية. ثم تقيم جميع العز لات لمدى لحساسيها للمصادات الحيوية بطريقة تخفيف الأجار. التنابح: من بين 600 مريض في المستشفيات من الجبهة ، صنار أذن ، إبط ، أصابع يد و أصابع قدم لعزول أصحات المظهرية والأنماط الور اثية. ثم تقيم جميع العز لات لمدى لحساسيها للمصادات الحيوية بطريقة تخفيف الأجار. التنابح: من بين 600 مريض في المستشفيات من مريض في المستمستما من من بين 100 مريض في المستشفى ، 79 (11.81٪) من مريضي كانت مستعمرة والتي عزلة منها 155 عزلة من الحمات منه منه ما التنابح: من بين 100 مريض في المتشفي ، 20 (11.81٪) من مريضي كانت مستعمرة والتي عزلة منها 155 عزلة من ما كمات الموالية لتنابح: من بين 100 مريض في المولية لتنبيط 20٪ و 20.9 (11.81٪) من مريضي كانت مستعمرة والتي عزلة منها 155 عزلة من التولي) كانت المنابح: المثلو عزن أكثر المضادي الجرفي في المستشفي و كان على التوالي كانت منه التنابح: من المولية لتنبيط 20٪ و 20 من التوالي) كانت على التولي) كانت ملوب النابع: من حلال الأردن ، المام الور التر أكم على من من مام على موالي عزل أكم على التوالي) كانت منا أكثر المضاد الحيوية فعالية مع حساب قدم مرور المنجر للمرغي كا لملوبة لتنبيط 20٪ و 20% من المز لات مع على التوالي) كانت مستملو عن أكثر المضادة الحيوية فعالية مع حساب قدم المن عالي المبطر في المبطري المثمان ال الم معنان أكثر المضادة الحيوية فعالية مع موال (لذن ، إلتر عام علم للمن الملوبة لتنبيط 20% مال على التوري فردي المرافي عالي التولي كان ملمما

الكلمات الدالة: مقاومة المصادات الحيوية، الاستعمار، مقاومة الأدوية المتعددة ، قيم التركيز المثبط/لأدني