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Research Article

Inappropriate Antibiotic Prescription for Acute Viral Respiratory Tract Infections in Egypt-Single Center Experience

Usama E Aboelhassan[1]*, Magda S Rezk[2], Tamer Saber[3] and Mohammed Al-Harrass[4]

[1]*Kasrlainy Faculty of Medicine, Cairo University Hospital, Cairo, Egypt*

[2] *MD of Anaesthesia and ICU, Cairo University, Egypt*

[3] *MD of Internal Medicine, Zagazig Univeristy, Egypt*

[4] *MD of Clinical Pathology, Mansoura University, Egypt*

***Corresponding Author:** Usama E Aboelhassan, Kasrlainy Faculty of Medicine, Cairo University Hospital, Cairo, Egypt.

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Abstract

Rationale: Antibiotic (AB) that prescribed inappropriately could accelerate the AB resistance. AB resistance represents a major health issue and will be of a great economic burden if not properly addressed. Data about the inappropriate antibiotic use of AB in Egypt is limited so the aim for this study to detect how frequent AB inappropriately prescribed for acute viral respiratory tract infections.

Methods: The current study was conducted at Cairo University Hospitals. It was conducted on hospitalized both adults as well as pediatric patients (age < 18 years old), over the period of 4 years from 2010 to 2014. All the patients who fulfilled the WHO case definition of sever acute respiratory tract infection (SARI) were enrolled. Demographic data, Clinical manifestations, co-morbid conditions and data about AB usage during the last week before admission to Hospital were collected. Nasopharyngeal (NP) and/or oropharyngeal (OP) swabs were collected and analyzed for the viral panel and atypical bacteria through PCR technique.

Results: Eligible patients who fulfilled the inclusion criteria were 3207. 1075 (33.5%) were found to be positive for viral and atypical bacteria, 912 (84.4%) women. The mean age among cases was 5.74 ± 13.87 years. Children less than 5 years represented 83% of the cases. Data about how frequent AB before admission was only available for 784 cases over 1075 positive cases. Almost 46% (360/784) of viral confirmed cases were received AB before admission. The most frequently used ABs were penicillin/cephalosporin/macrolides.

Conclusion: Inappropriate AB prescription was reported in 46% of the patients confirmed viral respiratory tract infection. The most frequently used AB were penicillins/cephalosporins/macrolides.

Keywords: *Inappropriate Antibiotics; Ambulatory; Acute Viral Respiratory Tract Infections; Cairo University Hospital*

Introduction

Inappropriate usage of AB presents a major concern despite much effort is being done to control this issue. Beside the huge economic burden for this problem, it will render the bacteria resistant to most of used AB. recent reports suggested that up to 40% of the patients with viral respiratory tract infections are given AB [1-3]. These patient who received inappropriate AB were at higher risk to develop complications from these AB such as severe allergic reaction [4].

Many countries through effective initiatives and through antibiotic stewardship programs have achieved good promising results in controlling over prescription for respiratory tract infections especially for children. Also, it was noted that intervention like vaccination play an important role according to recent reports; for example 7-valent pneumococcal conjugate vaccine (PCV-7) led to reduction of the rates of invasive disease due to antibiotic-resistant Streptococcus pneumonia [1,2-11].

According to our knowledge data about the inappropriate antibiotic use of AB in Egypt is limited so the aim for this study to detect how frequent AB overprescribed for viral causes of acute respiratory tract infections.

AB that prescribed inappropriately could accelerate the resistance dissemination and emergence. Such resistance dissemination represents a major health issue and will be of a great economic burden if not properly addressed.

Material and Methods

The current study was conducted at Cairo University Hospitals. It was conducted on hospitalized both adults as well as pediatric patients (age < 18 years old), over the period of 4 years from 2010 to 2014. All the patients who fulfilled the WHO case definition of SARI [12] were enrolled and admitted. Criteria used is; fever of ≥ 38°C or history of fever plus cough within the last 10 days.

Data for all eligible patients were collected through specific data collection form including demographic data, Clinical manifestations, co-morbid conditions, AB usage during the last week before admission to Hospital were recorded.

Nasopharyngeal and oropharyngeal swabs were collected and analyzed for the following viral panel and atypical bacteria. Viral panel includes; pandemic influenza 2009 A (H1N1), seasonal H1, and H3. RSV, PIV, hMPV, adenovirus, rhinovirus, Boca alongside while atypical bacterial panel includes that includes (*Mycoplasma/Legionella/Chlamydia*). Sputum for gram stain with culture and sensitivity could not be collected for all patients.

Kits used for PCR viral and atypical bacteria analysis are a MagMAX Total Nucleic Acid Isolation Kit (Cat No. ARE 1840; Applied Biosystems, Foster City, California, USA).

Ethical standards

Formal written consent was obtained either from patients themselves or by patients sponsors. Study protocol was approved by Cairo university ethics committee and is consistent with Helsinki Declaration of Bioethics protocol [13].

Statistical analysis

Data were statistically described in terms of mean ± standard deviation (± SD), median and range, IQR, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student t test for independent samples. For comparing categorical data, Chi-square (c^2) test was performed. Exact test was used instead when the expected frequency is less than 5. P values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

Results

Eligible patients who fulfilled the inclusion criteria were 3207. 1075 (33.5%) were found to be positive for viral and atypical bacteria (cases), while 2132 (66.5%) were negative for both (controls). Cases included 912 (84.4%) women and 163 (15.6%) men. The mean age among cases was 5.74 ± 13.87 years, and 6.96 ± 25.38 years among controls, respectively (P < 0.001). Children less than 5 years represented 83% of the cases.

Characteristics	Total [n (%)]	Cases [n (%)]	Controls [n (%)]	OR (95% CI)	P value
Number	3207	1075 (33.5)	2132 (66.5)	0.116 (1.570 - 1.760)	< 0.001
Sex					
Females	1722 (53.7)	912 (84.8)	810 (47.1)	0.731 (8.600 - 10.857)	0.537
Males	1485 (46.3)	163 (15.2)	1322 (52.9)	1.285 (2.334 - 5.427)	< 0.001
Age (mean ± SD)	13.20 ± 22.82	5.74 ± 13.87	16.96 ± 25.38	0.831 (9.600 - 12.857)	< 0.001
Age groups (years)					
<18	2479 (77.3)	981 (91.2)	1493 (70.0)	4.407 (3.497 - 5.552)	< 0.001
<1	1347 (42)	520 (48.3)	831 (39.0)	1.466 (1.265 - 1.700)	< 0.001
1 - 5	949 (29.6)	374 (34.8)	567 (26.6)	1.716 (1.461 - 2.016)	< 0.001
>5	183 (5.7)	87 (8.1)	95 (4.4)	1.785 (1.324 - 2.407)	< 0.001
>18	728 (22.7)	94 (8.8)	639 (30.0)	0.226 (0.180 - 0.285)	< 0.001

Table 1: *Demonstrates these demographic data.*
CI: Confidence Interval; OR: Odds Ratio.s

We found that RSV (485 cases, 45.2%), PIV (125, 11.6%), and adenovirus (105, 9.8%). Single viral etiology was reported in 901 (83.3%) cases, while 174 (16.7%) cases had mixed etiologies. Children less than 18 years had a higher viral etiology (981 cases, 91.2%) compared with 94 (8.8%) cases in adults. Only three cases were positive for *Mycoplasma* spp. and were co infected with RSV. While only one case of *Chlamydia* spp. Was co infected with RSV and hMPV. Neither corona virus nor *Legionella* spp. Was detected.

	RSV	Adenovirus	Rhinovirus	Enterovirus	Infl	Bocavirus	hMPV	PIV	Mixed	Total [n (%)]
Age groups (years)										
< 18	470	97	12	1	47	11	70	111	162	981 (91.2)
< 1	269	29	0	0	23	5	43	59	73	501 (46.6)
1 - 5	165	52	10	1	17	5	22	46	66	384 (35.6)
> 5	36	16	2	0	7	1	5	6	23	96 (9.0)
> 18	15	8	0	30	0	0	7	14	12	94 (8.8)
Total	485	105	20	1	77	11	77	125	174	1075 (100)
Yearly distribution										
2010	221	26	0 0	0	11	0	11	45	40	354 (32.9)
2011	63	50	0	0	32	6	48	59		50 308 (28.6)
2012	127	25	0 0	0	19	2	13	17	31	234 (21.8)
2013	35	4	13	1	7	1	5	4	52	122 (11.4)
2014	39	0	7	0	8	2	0	0	1	57 (5.3)
	485 (45.2)	105 (9.8)	20 (1.8)	1 (0.0)	77 (7.2)	11 (1.0)	77 (7.2)	125 (11.6)	174 (16.2)	1075 (100)

Table 2: *Age and yearly distribution of detected viruses among the study cases.*

hMPV: Human Metapneumovirus; Infl: Influenza virus; mixed, more than one virus; PIV: Parainfluenza Virus; RSV: Respiratory Syncytial Virus.

Data only available for 784 cases from the total number of positive cases 1075. Table 3 showed the total number of cases who received AB before admission to the hospital the number of positive viral respiratory tract infections received AB before admission. Almost 46% (360/784) of viral respiratory tract infections confirmed cases received AB before admission. The most frequently used AB were penicillins/cephalosporins/macrolides.

Crosstab					
		Negative cases	Group		Total
			Positive cases		
Antibiot	No	Count	1,024	424	1,448
		% within Antibiot	70.7%	29.3%	100.0%
		% within Group	66.8%	54.1%	62.5%
	Yes	Count	509	360	869
		% within Antibiot	58.6%	41.4%	100.0%
		% within Group	33.2%	45.9%	37.5%
Total		Count	1,533	784	2,317
% within Antibiot		66.2%	33.8%	100.0%	
% within Group		100.0%	100.0%	100.0%	

Table 3: Total no. received AB before hospital admission.

This group of patient who has received AB before admission has been distributed as 44% (158/360) male while 56% (202/360) were female none of them was pregnant. patients less than 18 years of age were 97% (351/360) where older than 18 years were only 3% (9/360). NP swab were taken from all these patients while 356 throat swabs were collected.

They had viral infections distribution as follows (167 RSV/69 mixed/31 adeno virus/hMPV 30/PIV 30/18 influenza/12 Rhino virus/2 Boca virus/1 entero virus). Almost 50% (180/360) of cases who received inappropriate AB had chronic disease distributed as from the most common problem to less common (asthma/cardiac/other respiratory/neurological/endocrinal/hepatic/ renal/hematological) while other 49% (178/360) of cases did not have any chronic problems while 1% (2/360) were unknown to have any chronic problems.

In this study 28% (102/360) of the patients had white blood count (WBC) more than 11.000 cells per cubic millimeter of blood, 2% (7/360) patients had WBC less than 3.000 cells per cubic millimeter while 70% (250/360) of patients had WBC within normal. CXR was abnormal in 83% (302/360) of the patients who received inappropriate AB. In this patient group there 83 cases had been admitted to ICU and MV applied for 38 cases. In this study 10% (37/360) of these cases had o2 SAT ≤ 90%. Almost 95% (342/360) of these cases discharged from the hospital, 3.6% (13/360) cases died while data unavailable for 1.4% (5/360).

Discussion

This prospective descriptive study is a part from large study conducted over 4 years in Cairo university hospitals for surveillance of viral and atypical bacteria in both children and adult populations. One of the secondary outcomes that had been estimated during this work is to know how frequent AB had been prescribed inappropriately on ambulatory base before admission. This study showed that 46% of the confirmed viral respiratory tract infections cases have been prescribed AB inappropriately.

Evidence before this study

According to our knowledge; data in Egypt is very limited on how frequently AB prescribed inappropriately for respiratory tract infection as outpatient's base. This study showed 46% of the patients with confirmed viral respiratory tract infections had been received AB inappropriately. This is consistent with the study done by Barlam T., *et al.* [3] who concluded that 40% of AB were unnecessary. Another study have detected that 30% of the patients received inappropriate AB [15], another study included 1000 adults with respiratory tract infections detected that 64% of the patients had been received inappropriate AB [16].

The problem of inappropriate use of AB may result in emergence of resistance due to selective pressure on microorganisms upon to exposure to specific antimicrobial agent [17]. Also, inappropriate use of AB could accelerate the resistance dissemination. We believe that to properly control resistance emergence and dissemination there are many actions should be considered: 1) to develop stewardship program that adopt the prudent use of AB and to lower antimicrobial consumption 2) infection control prevention interventions 3) effective vaccination programs.

Infections with such possible resistant microorganisms have direct and indirect effects on health system. Direct effects on health system include longer length of stay, longer illness period, and increase mortality with increase cost where indirect effects include economic losses due to decrease productivity caused by longer sickness stage [22].

What is behind this pattern of prescription of AB as outpatients or ambulatory base in Egypt in not exactly addressed and needs further research but may raise many concerns. First concern: Any knowledge gaps are there as regard prescription guidelines and indications for AB prescription. second concern: Egyptian patients expectations about AB prescription and this point needs further larger study to be assessed properly; As U.S studies showed AB providers has higher expectations for AB prescription to their patients than actually there as shown by Francois Watkins LK., *et al.* "The physicians expected that 54% of their patients seeking for AB but 26% only of the patients expected that [18]". The third concern: is there any urgent indication to establish national standards or guidelines or even simple pathways for AB prescription showing when to start this AB and for how long this AB will continue. As Jenkins., *et al.* showed that following pathways for AB prescription has been associated with reduction of AB prescription for respiratory tract infections [19]. Also Yogo., *et al.* showed that these clinical pathways may the minimum effective duration for AB and he also showed that pharmacist may play a good role for adherence for this duration [20]. Fourth and last concern: it will be possible and feasible to adopt delayed AB prescription strategy or not, as this approach May safely decrease antimicrobial use when used in conjugation with guidelines [21].

We think that there are some important interventions on higher levels might be considered to prevent this pattern from progression and to decrease possible AB resistance; these interventions may include:

1) Possible written justifications for AB on the medical record [23].
2) Proper communications skill for physician and educate them how he/she can persuade the patients about the harms that he/she may predispose himself/herself in a case of inappropriate AB [24-26].

We believe that patient education through different sources like media or internet represents an important role to decrease this pattern.

Also, many report address the potential role for clinician antimicrobial prescribing Tracking and reporting may play also an important role as many reports showed that [9,23,27] but we think this will be a difficult unfeasible approach.

Conclusion

Inappropriate AB perception was reported in 46% of the patients with confirmed viral respiratory tract infection by PCR. The most frequently used AB were penicillins/cephalosporins/macrolides. Action should be taken as early as possible to increase awareness of clinicians and general orientation to the patients about the danger inappropriate AB prescription.

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