

CHARLES UNIVERSITY IN PRAGUE
CZECH REPUBLIC

Faculty of Pharmacy – Hradec Kralove

Department of Social and Clinical Pharmacy

PhD Thesis

Hradec Kralove, 2014

Pharm Dr. Abobakr Abasaheed

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**Analysis of the Use of Antibiotics in the
United Arab Emirates**

PhD Thesis

Supervisor: Prof. Jiri Vlcek

Hradec Kralove, 2014

Pharm Dr. Abobakr Abasaheed

Dedication

*With humility and reverence, this work is dedicated to my late
Father
Mother
&
My Brothers Hashim & Abbass
as well as my dear friend Abdul Rahman.
May their souls rest in peace and enjoy the promised paradise*

*A special gratitude to my affectionate brother and Godfather “Hassan” who
has overwhelmed me with his passion, valuable advices and stretched arms.*

*My sincere appreciation to my partner in life and caring wife Dr.Maha, and
my beloved children Shahad, Sara and Mohammed for their concern and
love.*

*The gratitude is extended to my brothers and sisters for their spiritual support
and encouragement, and all my friends and colleagues.*

Motto:-

“The trouble with being a hypochondriac these days is that antibiotics have cured all the good diseases”

Caskie Stinnett
1911

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Last but not least, I would like to pass my regards and blessings to all of those who supported me in any respect during the completion of the project.

Declaration

I declare this thesis is my individual work, which I have developed on my own. All literature and other sources of information which I used in processing are included in the list of references and quoted properly.

PharmD. Abobakr Abasaed

In Hradci Králové, 2014

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ABBREVIATIONS

ADNOC	:	Abu Dhabi National Oil Company
ADRs	:	Adverse Drug Reaction
AED	:	Arab Emirates Dirham
APUA	:	The Alliance for the Prudent Use of Antibiotics
ATTAIN	:	Assessment of Telavancin for Treatment of Hospital-Acquired Pneumonia
ATB	:	Antibiotics
ATC	:	Anatomical Therapeutic Chemical Classification
CA	:	Community-Acquired
CAP	:	Community-Acquired Pneumonia
CD-A	:	Controlled Drugs- Control Drug Class A
CD-B	:	Controlled Drugs- Control Drug Class B
CDC	:	Centers for Disease Control and Prevention
CO₂	:	Carbon Dioxide
CVD	:	Cardiovascular Diseases
DALYs	:	Disability Adjusted Life Years
DDD	:	Defined Daily Dose
DHA	:	Dubai Health Authority
DHCC	:	Dubai Healthcare City
DNA	:	Deoxyribonucleic Acid
DOHMS	:	Department of Health and Medical Services
EARSS	:	European Antimicrobial Resistance Surveillance System
ESAC	:	European Surveillance of Antimicrobial Consumption
ESBL	:	Extended Spectrum Beta Lactamases
EU	:	European Union
GAHS	:	General Authority for Health Services for the Emirate of Abu Dhabi
GDP	:	Gross Domestic Product

GCC	: Gulf Co-Operation Council
GIT	: Gastro Intestinal Tract
GNP	: Goss National Product Per Capita
GSLS	: General Sale List For Supermarket
HAAD	: Health Authority of Abu Dhabi
HAP	: Hospital-Acquired Pneumonia
HCPs	: Health Care Providers
INCB	: International Narcotic Control Bureau
NRUD	: The International Network For Rational Use Of Drugs
MBC	: Minimum Bactericidal Concentration
MIC	: Minimum Inhibitory Concentration
MoA	: Mode of Action
MOH	: Ministry of Health
MRSA	: Methicillin-Resistant Staphylococcus Aureus
NIH	: National Institutes of Health
OTC	: Over the Counter
OTC-G	: Medicines sold in Pharmacy & Non Pharmacy Outlet
OTC-P	: Over the Counter Pharmacy Medicines
P	: Pharmacy Medicines
PABA	: Para-Amino Benzoic Acid
PAE	: Post-Antibiotics Effect
PBPs	: Penicillin-Binding Proteins
PCV7	: Pneumococcal Vaccine
PDD	: Prescribed Daily Dose
PH	: Power of Hydrogen
PHCs	: Primary Healthcare Centers
PHOM	: Medicines Restricted to Pharmacies only
PK/PD	: Pharmacokinetics / Pharmacodynamics
POM	: Prescription Only Medicines
RDT	: Rapid Diagnostic Test
RNA	: Ribonucleic Acid

SBT : Serum Bactericidal Titer
STD : Sexually Transmitted Disease
TB : Tuberculosis
UAE : United Arab Emirates
UK : United Kingdom
US : United State of America
WHO : World Health Organization

TABLE OF CONTENT

Acknowledgment

Abbreviations

1. Introduction	1
2. Aims of the Research	3
3. Glimpse about the UAE	5
3.1 Location and population	5
3.2 The UAE Healthcare System	7
3.2.1 Federal Healthcare Management	11
3.2.2 Local Healthcare Management	11
3.2.3 Private Healthcare System	12
3.2.3.1 Dubai Healthcare City	12
3.3 Healthcare insurance	12
3.4 Pharmaceutical sector in the UAE	13
3.4.1 Dispensing Mode of Medicine	16
3.4.1.1 Controlled drugs-Narcotics	16
3.4.1.2 Medicine by prescription Only (POM)	16
3.4.1.3 Medicine Restricted to Pharmacists Only (PH-OM)	17
3.4.1.4 Over the counter Pharmacy Medicine (OTC-P)	17
3.4.1.5 Medicine sold in Pharmacy and Non Pharmacy outlet (OTC-G)	17
4. Theoretical Part	18
4.1 Definition of Antibiotics	19
4.2 Characteristics	19
4.3 Mechanisms of Action of Antibiotics	21

4.4 Post- antibiotic effect	22
4.5 The role of Antibiotics	23
4.5.1 Therapeutic Indications	23
4.5.2 Prophylactic Indications	24
4.6 Why Are Antibiotics important?	24
4.7 Risks of Antibiotics Use	26
4.7.1 Adverse Drug Reactions	26
4.7.2 Drug Interactions	29
4.7.3 Super Infections	31
4.7.4 Antibiotics Resistance	32
4.7.4.1 What is Antibiotics Resistance?	32
4.7.4.2 Causes of Antibiotics Resistance	33
4.7.4.2.1 Reasons Related to Antibiotics Use	33
4.7.4.2.2 Reasons Related to Investment in Research.	34
4.7.4.3 Mechanisms of Antibiotics Resistance	35
4.7.4.4 Cost of Antibiotics Resistance	36
4.7.4.5 Strategies to Over-Come Antibiotics Resistance	36
4.8 Factors influencing Antibiotics Use	40
4.9 Newly invented and in the pipeline antibiotic agents	44
5. Practical Part	48
5.1 Study I: Attitudes towards antibiotics use among banking employees in Sudan, Oman and UAE	49
5.1.1 Background	49
5.1.2 Objectives	49
5.1.3 Methods	50

5.1.3.1 Study Design	50
5.1.3.2 Study Setting	50
5.1.3.3 Study Population	50
5.1.3.4 Data Collection	50
5.1.3.5 Statistical Analysis	51
5.1.4 Results	51
5.1.5 Discussion	60
5.1.6 Limitation of the Study	62
5.1.7 Conclusion	62
5.2 Study II: Self-Medication with antibiotics by the community of Abu Dhabi Emirate, United Arab Emirates (UAE)	63
5.2.1 Introduction	63
5.2.2 Objectives	65
5.2.3 Methods	65
5.2.3.1 Setting	65
5.2.3.2 Study Population and Sample Size	66
5.2.3.3 Data Collection	66
5.2.3.4 Statistical Analysis	66
5.2.4 Results	67
5.2.5 Discussion	74
5.2.6 Limitations of the Study	76
5.2.7 Conclusion	77
5.3 Study III: A comparative study between prescribed and over- the counter antibiotics	78
5.3.1 Introduction	78

5.3.2 Objectives	79
5.3.3 Methods	80
5.3.3.1 Study Design	80
5.3.3.2 Study Setting	80
5.3.3.3 Sample Size	81
5.3.3.4 Data Collection	81
5.3.3.5 Statistical Analysis	83
5.3.4 Results	83
5.3.5 Discussion	94
5.3.6 Limitations of the Study	97
5.3.7 Conclusion	97
6. Abstract	99
7. Abstrakt	105
8. Conclusion	110
9. List of tables	112
10. Lists of Figures and Maps	114
11. List of Publications, Presentations and invented speech	115
12. Appendices	118
12.1 Appendix 1: Use of Antibiotics Questionnaire	118
12.2 Appendix 2: List of Commonly used Antibiotics	126
12.3 Appendix 3: Abu Dhabi Health Authority Approval	127
12.4 Appendix 4: Portrait of the Commonly Used Antibiotics	128
12.5 Appendix 5: Abu Dhabi Health Authority Approval	129
12.6 Appendix 6: Pharmacist Information Sheet	130

12.7 Appendix 7: Pharmacist Consent Form	131
12.8 Appendix 8: Questionnaire of Study III	132
13. References	134

1.0 Introduction

The misuse of antibiotics for viral infections (for which they are of no value) and the immoderate use of broad spectrum antibiotics instead of narrower spectrum antibiotics have been well-documented and reported. Therefore the inappropriate use of antibiotics is getting a global problem, mainly in the developing countries ^[1,2]. Many factors have contributed to this problem such as improper drug selection, inappropriate dosage (over-use and under-use), patient non-compliance and practitioner type and specialty ^[3, 4, 5].

Despite the abundance of safe, effective and low-cost antibiotics since mid 20th century, resistance to existing antibiotics has recently become widespread and created a great challenge to public health in the 21st century ^[6, 7]. Previously, antibiotics resistance was thought to be an isolated hospitals problem due to nosocomial infections, long stay of patients and nursing homes. However, recently the proportion of community-acquired (CA) infections with bacteria resistant to antibiotics has increased ^[8,9]. Emergence of antibiotics resistance is often a result of irrational prescribing patterns, misuse of the antibiotics as well as self-medication.

Recognition of the severity of antibiotics resistance in both developed and developing countries by medical, public health, scientific leaders and health organization worldwide leads them to developed national and regional surveillance systems to track the spread of hospital- and CA antibiotic resistance, raise problem awareness and stimulate governments to take action through policy interventions (Mossialos et al ., 2008)^[10]. For instance, in 2006 the European Antimicrobial Resistance Surveillance System (EARSS) reported that pathogens resistant to penicillin occurred in up to 25.0-50.0 % of isolates in

France, Spain, and Romania, 24.0%, 25.0%.88.0%; respectively ^[10, 11]. The United States of America (USA) Centers for Disease Control and Prevention (CDC) declared that

antimicrobial resistance is currently one of the most pressing public health issues in the US [12].

Although the United Arab Emirates (UAE) antimicrobial policy restricts dispensing of antibiotics without prescription [13], studies revealed the wide availability of these agents over the counter (OTC), their over prescribing pattern and the high prevalence of self-medication with antibiotics [14, 15] unfortunately and regardless of this results, there is a lack and paucity in studies that tracking the prevalence of antibiotics resistance [16, 17].

World Health Organization (WHO) confesses that antimicrobial resistance is not just a country-level challenging problem, but it is a global and international issue [18]. During the last decades the UAE has become the focus of researchers attention where we find that there is a tremendous increase in the volume of trade, travel and immigration, which led to a change in the population structure in terms of ethnic diversity and therefore social and cultural changes and these certainly will be a key factors in the spread and increase of the resistance of pathogenic bacteria..

To minimize the susceptible rates of resistance and for better evaluation of the benefits and risks of antibiotics, it's not suffice to assess only the patient's attitude (self-medication with antibiotics) and the prescribing patterns ,but it's very important to consider the well-established, but complex relationship between the consumption and utilization of antibiotics and the prevalence of the resistance to them.

Sequence of studies in this research shed light on this problem. This was especially in studies of the consumption and drug utilization and rational use of medicine and as well exemplified by the experience of the European Surveillance of Antimicrobial Consumption (ESAC) [19].

2. Aims

Self-medication and over the counter use of antibiotics is believed to be highly associated with the emergence of antibiotic resistance. For this reason and since this practice has a long history the in UAE, series of pharmaco-epidemiological studies were carried-out to evaluate the use of antibiotics in terms of self-medication, prescribing and dispensing patterns in UAE. The research results will serve as platform for strict and solid interventions for better use of antibiotics. The following were the objectives of the research:

- To evaluate the attitude of certain cohort (banking employees) of the community towards use of antibiotic (Study I).
- To estimate the prevalence of self-medication with antibiotics in Abu Dhabi. (Study II).
- To identify Abu Dhabi community socio-demographic factors related to self-medication with antibiotics (study II).
- To Identify types of Antibiotics used for self-medication. (study II).
- To characterize the sources of obtaining antibiotics without prescriptions and the reasons for their use (study II).
- To realize the relationship between intended self-medication, storage, and actual self medication (study II).
- To examine the impact of demographic characteristics (age,gender and years of work experience) of the pharmacist with respect to dispensing antibiotics (with and/or without prescription) in terms of legalization, rationality and safety (Study III).

- To study the pattern of dispensing antibiotics (with and/or without prescription) in terms of frequency, costs and indications i.e. reasons for dispensing (Study III).

3. GLIMPSE ABOUT UAE

3.1 Location and population

United Arab Emirates (UAE) is located in the Middle East region of Asia. It is at the tip of the Arabian Peninsula, having borders with Saudi Arabia and Oman and is one of the GCC (Gulf Co-operation Council) States, and is comprises of seven emirates. The UAE seven emirates federation was officially announced on 2nd December 1971. The estimated population is 8,264,070 million people ^[20] (**Table1**), comprised of different ethnic groups (88.5 % are expatriates) ^[21]. The Nominal gross domestic product (GDP) in 2011 was 360 billion \$ and the product gross national product per capita (GNP) is \$ 41,550 ^[22].

MAP 1- United Arab Emirates map



Table 1-A UAE National population by Emirate and sex (2010 midyear estimates)

Emirate	Male	Female	Total
Abu Dhabi	204,108	200,438	404,546
Dubai	84,245	83,784	168,029
Sharjah	78,818	74,547	153,365
Ajman	21,600	20,586	42,186
Umm Al-Quwain	8,671	8,811	17,482
Ras Al Khaimah	49,181	48,348	97,529
Fujairah	32,486	32,374	64,860
Total	479,109	467,888	947,997

Table 1-B Population by Nationality (National-Non National) and sex (2010 midyear estimates)

Nationality	Male	Female	Total
National	479,109	468,888	947,997
Non-National	5,682,711	1,633,362	7,316,073
Total	6,161,820	2,102,250	8,264,070

*** The table is cited from: National Bureau of Statistics*

²⁰⁻ (Uaestatistics.gov.ae. Report Details [Internet]. 2014 [11 June 2014]. Available from: <http://www.uaestatistics.gov.ae/EnglishHome/ReportDetailsEnglish/tabid/121/Default.aspx?ItemId=1914&PTID=104&MenuId=1>)

3.2 The UAE Healthcare System

In the early seventies, there were only 7 hospitals and 12 primary healthcare centers (PHCs) within the UAE, which reflect the limitations of healthcare facilities throughout the country. ^[23] In 2000, The World Health Organization (WHO) ranked the UAE healthcare system 27th best out of 191 countries, ^[24]. The standards of health care in the UAE are generally high, reflecting the high level of public spending over the decades since the oil boom. The provision of best healthcare has been reflected in rapidly improving figures for key indicators such as life expectancy and infant mortality rates ^[25] **(Table 2)**, which are now considered equivalent to western levels ^[26] The latest released statistics by the National Bureau of Statistics (UAE) indicated the following:

- There were 33 governmental hospitals and 269 clinics and centers in 2011^[27] **(Table 3)**
- There were 65 private hospitals and 2927 clinics and centers in 2011. ^[27] **(Table 4)**

The enormous expansion in healthcare infrastructure created an extra management burden on the MOH authorities and hence necessitated the development of a new healthcare management system in the country that resulted in the partnership between the federal government and each emirate local authorities.

Table 2- Causes of Death in the UAE by Sex in 2011

Cause of Death	Sex	Age Group														Total		
		0-1	1-4 Yrs.	5-9 Yrs.	10-14 Yrs.	15-19 Yrs.	20-24 Yrs.	25-29 Yrs.	30-34 Yrs.	35-39 Yrs.	40-44 Yrs.	45-49 Yrs.	50-54 Yrs.	55-59 Yrs.	60-64 Yrs.		65+ Yrs.	Unspec.
CVD	M	17	5	2	2	9	18	42	67	90	106	126	164	130	121	468		1367
	F	12	6	2		3	6	10	9	8	18	20	28	33	31	396		582
Accidents	T	29	11	4	2	12	24	52	76	98	124	146	192	163	152	864	0	1949
	M	7	22	26	13	59	167	217	159	130	105	69	52	33	29	25	6	1119
Cancer	F	3	16	8	6	8	18	25	21	15	11	6	3	3	3	10	3	159
	T	10	38	34	19	67	185	242	180	145	116	75	55	36	32	35	9	1278
Pneumonia & Bronchitis	M	3	5	6	1	1	3	10	12	7	20	16	34	40	59	160	1	378
	F	1	4	3	1	0	1	6	11	21	15	37	37	38	44	133	1	353
Congenital Anomalies	T	4	9	9	2	1	4	16	23	28	35	53	71	78	103	293	2	731
	M	10	7	5	2	2	13	26	51	51	35	43	53	51	25	120		494
Diabetes Mellitus	F	8	3	3	1	2	1	5	3	5	5		11	4	11	95		157
	T	18	10	8	3	4	14	31	54	56	40	43	64	55	36	215	0	651
Septicemia	M	248	5	3	3	2	1											262
	F	188	12	3	2	1	1		1									208
Nephritis Nephrotic Syndrome & Nephrosis	T	436	17	6	5	3	2	0	1	0	0	0	0	0	0	0	0	470
	M		1						3	3	10	12	19	26	17	92		183
Not Stated	F				1					3	2	4	6	14	13	83		126
	T	0	1	0	1	0	0	0	3	6	12	16	25	40	30	175	0	309
All Other Causes	M	10	3			2	6	1	5	8	6	7	7	13	7	65		139
	F	8		1	1			2	3	1	3	3	6	3	12	69		112
TOTAL	T	18	3	1	1	2	6	3	8	9	9	9	13	16	19	134	0	251
	M	1	1		1			1	1	3	1		3	4	7	24		47
TOTAL	F								1	1		2	2	4	1	25		36
	T	1	1	0	1	0	0	1	2	4	1	2	5	8	8	49	0	83
TOTAL	M	5	5	3	5	9	29	56	53	50	68	68	81	50	34	66	81	663
	F	4	1	2		2	4	5	4	4	1	6	8	5	8	64	19	137
TOTAL	T	10	7	5	6	11	33	62	60	59	70	78	96	67	51	130	100	800
	M	23	18	4	6	6	23	59	55	56	62	55	53	43	34	135	1	633
TOTAL	F	14	9	3	2	7	11	8	15	14	9	12	9	16	24	106	0	259
	T	37	27	7	8	13	34	67	70	70	71	67	62	59	58	241	1	892
TOTAL	M	324	72	49	33	90	260	412	406	398	413	395	466	390	333	1155	89	5285
	F	238	51	25	14	23	42	61	68	72	64	90	110	120	147	981	23	2129
TOTAL	T	562	123	74	47	113	302	473	474	470	477	485	576	510	480	2136	112	7414

** The table is cited from:
 25- The Annual Report 2010 Health Policies Sector MoH UAE. UAE: MoH; 2010.

Table 3 Government Health Services Statistics 2007-2012 in the
UAE

Item	2012 ¹	2011 ¹	2010	2009	2008	2007
Hospitals	33	34	33	33	32	34
Beds	7,125	7,929	7,035	7,061	6,627	7,607
Clinics & Centres	xxx	269	271	277	243	197
Physicians	5,251	5,031	5,312	5,159	5,969	4,711
Dentists	625	549	659	610	526	566
Nurses	15,253	14,325	14,889	14,091	15,443	13,460

xxx Data not Available

1- ADNOC Data for the years 2011 & 2012 were calculated within the Private Sector.

*** The table is cited from: National Bureau of Statistics*

27- (Uaestatistics.gov.ae. Report Details [Internet]. 2014 [11 June 2014]. Available from: <http://www.uaestatistics.gov.ae/EnglishHome/ReportDetailsEnglish/tabid/121/Default.aspx?ItemId=2313&PTID=104&MenuId=1>

Table 4 Private Sector Health Services Statistics 2007-2012 in the UAE

Item	2012 ¹	2011 ¹	2010	2009	2008	2007
Hospitals	65	58	53	59	58	51
Beds	3,494	2,556	2,557	2,665	2,549	2,076
Clinics & Centers	...	2,927	2,394	2,087	2,057	2,135
Physicians	11,166	7,866	7,440	6,847	7,342	5,412
Dentists	3,557	2,126	2,257	2,408	2,412	1,879
Nurses	15,736	10,611	9,473	7,948	8,688	3,876

... Not Available

1- ADNOC Data for the years 2011 & 2012 were calculated within the Private Sector.

*** The table is cited from: National Bureau of Statistics*

27- (Uaestatistics.gov.ae. Report Details [Internet]. 2014 [11 June 2014]. Available from: <http://www.uaestatistics.gov.ae/EnglishHome/ReportDetailsEnglish/tabid/121/Default.aspx?ItemId=2313&PTID=104&MenuId=1>

3.2.1 Federal Healthcare Management

The Ministry of Health (MOH) manages government-run hospitals and PHCs, including their private counterparts, in all emirates except Abu Dhabi and Dubai emirates, where local authorities are responsible for their management.

3.2.2 Local Healthcare Management

This system of management is applied in the emirates of Abu Dhabi and Dubai. Dubai emirate has established its Department of Health and Medical Services (DOHMS), which recently has been renamed as Dubai Health Authority (DHA). In 2001^[28], the Emirate of Abu Dhabi announced the formation of its local healthcare authority (General Authority for Health Services for the Emirate of Abu Dhabi (GAHS). In 2007 GAHS has been restructured into two organizations, the Abu Dhabi Health Authority (HAAD) and Abu Dhabi Health Services Company (SEHA)

3.2.3 Private Health care System

3.2.3.1 Dubai Healthcare City

The Government of Dubai has developed Dubai Healthcare City (DHCC), with the goal of creating a regional centre of excellence for medical services, medical education, and life sciences research in the Middle East. DHCC has international links with highly reputed global educational and research institutions.

DHCC is to become the internationally recognized location of choice for quality healthcare and an integrated centre of excellence for clinical and wellness services, medical education and research. The Medical Community is also home to the Mohamed Bin Rashid Al Maktoum Academic Medical Centre with the integration of its entities, many of which have USA origins: the Harvard Medical School Dubai Centre (HMSDC) Institute for Postgraduate Education and Medical research; the University Teaching Hospital (UH); the Dubai Harvard Foundation for Medical research (DHFMR); Boston University Institute for Dental Research & Education Dubai (BUIDRE); and Al Maktoum Harvard Medical Library.^[29]

3.3 Health Insurance

Until May 2003, all resident regardless of their nationality were entitled to comprehensive free healthcare services. However, these services have been suspended due to financial considerations. Since then, non-GCC (Gulf Countries Citizens) nationals have had to pay a pre-determined sum for each provided service.

In September 2005, GAHS launched a local health insurance scheme and it became mandatory, which obligated all the employers and business owners in the emirate of Abu Dhabi to cover the cost health care insurance for their expatriate employees and their families. A national health insurance company has been established for this purpose, which

was named (Daman) ^[30] this venture embodied a signpost in the history of healthcare for the Emirate of Abu Dhabi.

Three years later, in the middle of year 2008 a new health insurance program “Thiqa” (or “trust”) has been announced. Thiqa program was designed to provide UAE nationals a wide-range of healthcare services at all public and private healthcare facilities. Since national statistics shows high prevalence of hypertension and diabetes in UAE (diabetes estimated by 19 % these indicators led to “Weqaya” (or “protection”) program offered by, HAAD and SEHA ^[31] to predict risk factors for developing hypertension, diabetes and hypercholesterolaemia through free Weqaya health checks performed every two years. Cost of health services listed within the Daman scheme for the UAE nationals, is covered by Abu Dhabi government, while Non-UAE nationals can approach public hospitals and clinics of SEHA in the Abu Dhabi Emirate through their Daman and other insurance companies health cards ^[30] MOH established a new department for health insurance with responsibility to regulate and implements the health insurance system throughout the country. A drafted UAE Federal law on health insurance has been submitted to the UAE Ministers’ Cabinet for further discussion and approval.

Dubai Emirate started implementation of the health insurance program in February 2014.

3.4 Pharmaceutical sector in the UAE

Pharmacy sector in the UAE is rapidly progressing. There are definite strengths in UAE pharmacy system for example; the pharmaceutical industry and pharmacy practice has been included in the UAE Federal Law since the early 1980s. The principal legislation that regulates pharmaceuticals and pharmacy practice in the country is the UAE Federal Law number 4 of 1983 for Pharmaceutical Professions and Institutions .This law is not obviously identifying the tasks and responsibilities of pharmacist; but article 16 has stated some guidance for the pharmacist’s profession.

Synopsis of “Law 4/1983/ Article 16

The licensed pharmacist should carry out his duties in conformity with regulations of the profession and in particular:

- *Shall not conduct any practices against the honor of the profession.*
- *Shall keep confidential the disease, which he may come to know through the medical prescription presented to him or through any means related to his practicing of his work.*
- *Shall abide by the laws and regulations followed in this profession.*
- *Shall notify the communicable diseases he may discover during practicing his duties.*
- *Should not undertake himself any work other than his work in the pharmacy’’*

Although the numbers of pharmacists in the UAE are increasing, there is yet a shortage of pharmacists required to fulfill retail, hospital, industry, government and teaching positions in the country. **(Table 5)**

Table 5 - Numbers and Distribution of Community Pharmacies in the UAE

UAE Region	No. of Pharmacies	% of Pharmacies	No. of Pharmacists	% of Pharmacists	No. of Pharmacy Technicians	% of Pharmacy Technicians
Abu Dhabi	520	29.99%	1305	29.70%	426	25.32%
Dubai	560	32.30%	1572	36.90%	619	36.81%
Sharjah	382	22.03%	708	19.40%	375	22.29%
Ajman	120	6.92%	225	5.80%	116	6.90%
Umm Al Qiveen	18	1.04%	41	1.00%	12	0.71%
Fujairah	47	2.70%	87	1.80%	53	3.15%
Ras Al Khaimah	87	5.02%	167	5.40%	81	4.82%
Total	1734	100.00%	4103	100.00%	1682	100%

*** Data not published. Has been obtained on personal request from: Ministry of Health Drug Control Department- UAE*

3.4.1 Dispensing Mode of Medicines

In 2011 a ministerial decree No. MoH 922/2011 released and base on that, MOH re-classified and revised dispensing mode for the medicinal products in UAE therefore as per this new revision all drugs are now classified to the under one of the following categories

(32)

3.4.1.1 Controlled Drugs- Narcotics:

This group included medicines, which are controlled according to the regulation of the International Narcotic Control Bureau (INCB). Dispensation /supply is only in hospitals, through Narcotic Medical Prescription Form. This is valid for 28 days and must be issued by a consultant physician e.g. Amphetamines and other stimulants (such as methylphenidate), opioids (such as morphine and oxycodone) and others

3.4.1.1.1 Controlled Drugs- Class A (CD- A):

The dispensation of these medicines only upon” Special Control” white medical prescription, which is valid only for 3 days e.g.benzodiazepines,

3.4.1.1.2 Controlled Drugs- Class B (CD-B):

The dispensation of these medicines only upon” Special Control” white medical prescription, which is valid only for 3 days e.g. anti- depressants, anti-convulsants.

3.4.1.2 Medicines by prescriptions only (POM):-

These medicinal products must be dispensed by a licensed pharmacist (in pharmacy) only upon receiving a prescription from a legitimate healthcare professional (Physician).

3.4.1.3 Medicines Restricted to pharmacist only (PH-OM):-

These medicinal products must be dispensed by a licensed pharmacist (in a pharmacy); however a prescription from a physician is not required. Such products must not be stored in a direct access to consumers.

3.4.1.4 Over the counter Pharmacy Medicines (OTC-P):-

These medicinal products may be dispensed without a prescription and sold only in pharmacies. Such products may be stored in direct access to consumers.

3.4.1.5 Medicines Sold in Pharmacy & Non Pharmacy Outlet (OTC-G):-

These medicinal products may be sold in pharmacies and outlets such as supermarkets with controlled storage conditions. Acquisition must be made through licensed medical store only.

Despite, some parts of the pharmaceutical legislation are inclusive; they can only be effective to the extent that they are adhered to. For example the law restricted the sale of all prescription medicines without prescriptions. However in reality strict adherence to the law only applies to some medications like narcotics, hypnotics, tranquilizers and other agents that can cause dependence and addiction, therefore there is a wide range of prescription medicines including antibiotics, asthma inhalers, insulin and other anti-diabetics, cholesterol lowering and anti-hypertensive are commonly sold as OTC.

THEORETICAL PART

4.1 Definition of Antibiotics:

Antimicrobials have revolutionized the treatment of infectious disease revolving life-threatening diseases into more manageable and treatable conditions. In general antimicrobials are medicinal products that kill or stop the growth of living micro organisms and include antibacterial agents (more commonly referred to as antibiotics which are active against bacterial infections). Antimicrobials are different from antibiotics in that they can be either natural or synthetic substances which kill or inhibit the growth of viruses, fungi and parasites in addition to bacteria. ^[33, 34]Antibiotics are originally natural products, made from either bacteria or fungi, which kill or inhibit the growth of bacteria which causes diverse diseases.

According to ATC/DDD: Antibiotics' are all substances of ATC group 'J01' (Antibiotics for systemic use). 'Antimicrobials' are all substances of ATC group 'J'(anti-infective for systemic use, including antibiotics for systemic use, antimycotics for systemic use, antimycobacterials, antivirals for systemic use, immune sera, immunoglobulins and vaccines. Antiparasitic products (antiprotozoals, antihelminthics and ectoparasiticides) are assigned to ATC group 'P' and are thus not included. ^[35]

4.2 Characteristics

Despite the diversity of antibiotics with regard to their physical, chemical structure, pharmacological property and mechanism of action, all exhibited and excrete their selective toxicity to be effective in treating the infections without being harmful to the host, based on this diversity, antibiotics can be classified into the followings:

Bacteriostatic Versus Bactericidal Drugs

Antimicrobial drugs are classified as either bacteriostatic or bactericidal. For such bacterial activity the in vitro tests are very important, therefore; many microbiological techniques are used to determine the bactericidal activity of antibacterial agents against different isolates including the minimum bactericidal concentration (MBC), time-kill curve, and

serum bactericidal titer (SBT) as well as minimum inhibitory concentration (MIC) for bacteriostatic activity

Bacteriostatic agents: arrest the growth and replication of bacteria at serum levels achievable in the patient, thus limiting the spread of infection while the body's immune system attacks, immobilizes, and eliminates the pathogens.

Bactericidal agents: kills bacteria and the total number of viable organisms' decreases. ^{[36,}

37]

Chemotherapeutic spectra

The chemotherapeutic spectrum of a particular drug refers to the species of organisms affected by that drug.

Narrow spectrum

Chemotherapeutic agents acting only on a single or limited group of microorganisms are said to have a narrow spectrum. For example, Isoniazide is active only against Mycobacteria species.

Extended spectrum

Extended spectrum is the term applied to antibiotics that are effective against gram-positive organisms and also against a significant number of gram-negative bacteria. For example, ampicillin is considered to have an extended spectrum because it acts against gram-positive and some gram-negative bacteria.

Broad spectrum

Drugs such as tetracycline of broad spectrum antibiotics can drastically alter the nature of the normal bacterial flora resulting in a super infection of an organism. ^[19]

4.3 Mechanism of action of antibiotics

- **Inhibition of cell wall synthesis**

β -lactam and glycopeptides interferes with the production of peptidoglycan (layer in the bacterial cell wall) by binding to bacterial enzymes known as penicillin-binding proteins (PBPs). or transpeptidases; which in turn inhibits the final transpeptidation peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. ^[38]

- **Inhibition of protein synthesis:**

Interferes with bacterial protein synthesis by binding to 30S and 50S ribosomal subunits resulting in a defective bacterial cell membrane , The target of agents acting through this mechanism (aminoglycosides , tetracycline , spectinomycin , chloramphenicol , erythromycin, clindamycin, linezolid, Fusidic acid) is the polysomes (polyribosomes) in the bacterial cytoplasm. Depending on the agent, these may or may not be degraded. ^[39]

- **Folate Antagonists**

Because of their structural similarity to Para-Amino Benzoic Acid (PABA) they interfere with bacterial growth by inhibiting bacterial folic acid synthesis through competitive antagonism of PABA, resulting in inhibition of Folate synthesis (Sulfamethoxazole) or Folate reduction (Trimethoprim) or both (Co-trimoxazole) ^[40]

- **Inhibition of nucleic acid function or synthesis**

- **Inhibition of bacterial DNA gyrase**

The fluoroquinolones, quinolones and nirtofurantoïn enter the cell by passive diffusion through water-filled protein channels (porins) in the outer membrane. Intracellularly, they uniquely inhibit the replication of bacterial DNA by interfering with the action of DNA gyrase (topoisomerase IV) during bacterial growth and reproduction.

- **Inhibition of bacterial RNA synthesis**

These agents inhibit bacterial RNA synthesis by binding to the beta subunit of DNA dependent RNA polymerase, resulting in blockage of RNA transcription (Rifampin)^[41,42]

4.4 Post-antibiotics effect: (PAE)

PAE is one characteristic of pharmacodynamics is defined as the delayed re-growth of bacteria following exposure to an antibiotic. In spite of the increasing interest in the PAE as an important parameter for its major clinical relevance in designing the antibiotic dosage regimen and frequency of administration of a drug, knowledge on this phenomenon is still incomplete, but has been suggested that an alteration of DNA function is possibly responsible for post antibiotic effect following the observation that most inhibitors of protein and nucleic acid synthesis (aminoglycosides, fluoroquinolones, tetracyclines, clindamycin ect.) induce long-term PAE against susceptible bacteria. Theoretically, the ability of an antibiotic to induce a PAE is a hallmark of an antibiotic since they use to preserve their effectiveness and ability to suppress the growth of the bacterium, despite the fall of their concentration below the Minimum Inhibitory Concentration (MIC) for the bacterium. Factors that affect the duration of the post antibiotic effect include duration of antibiotic exposure, the nature of the antibacterial drug and its concentration and the bacterial species, and also environmental factors such as temperature, pH, pO₂, growth medium.

Most antimicrobial agents produce a PAE when tested against gram-positive cocci.

However, beta-lactam antibiotics (except for imipenem) have a minimal against gram-negative bacilli, or even a negative PAE ^[43, 44, 45, 46, 47]

4.5 The role of antibiotics

The indication of antibiotics was noted as either therapeutic or prophylactic.

4.5.1 Therapeutic indication

Selection of the most appropriate antimicrobial agent requires knowledge of several factors. The use of antibiotics for treatment can be either for:

- **Specific therapy:** This is applicable only, when there is a certain isolated micro-organism known as causative agent with well recognized antibiotic susceptibility.
- **Empiric Therapy:** Some critically ill patients require empiric therapy, which is immediate administration of antibiotic(s) covering infections caused by both gram-positive and gram-negative microorganism.

For proper and ideal selection of antimicrobial agent to treat an infection, the following principles should be considered: ^[48, 49]

- **Identification of the organism and its drug sensitivity establishment:**
Rapid assessment of the nature of the organism using different methods for culture e.g. disk diffusion, rapid diagnostic tests (RDTs) etc.
- **The effect of the site of infection on the therapy:**
Adequate levels of an antibiotic must reach the site of infection in order for the invading microorganism to be effectively eradicated. Some natural barriers may cause inadequate penetration of the drug into certain tissues such as the brain, prostate, and bone, although inflammation can influence the response to drug therapy in these tissues.
- **Status of the patient:**
When selecting an antibiotic, attention must be paid to the condition of the patient in terms of his immune system, renal and hepatic function, pregnancy, lactation and age.

- **Safety of the agent:**

Many of the antibiotics, such as penicillin's, are among the least toxic of all drugs, because they interfere with a site unique to the growth of microorganisms. Other antimicrobial agents (for example-e.g., chloramphenicol) are less specific and reserved for life-threatening infections.

- **Cost of therapy:**

Often, several drugs may show similar efficacy in treating an infection, but vary widely in cost, example, the triple therapy regimen for eradicating the gram-negative bacillus *Helicobacter pylori*.

4.5.2 Prophylactic Indication:

Prophylaxis was defined as 'no evidence of infection at the start of the antibiotic course'

Certain clinical situations require the use of antibiotics for the prevention rather than the treatment of infections. Since the indiscriminate use of antimicrobial agents can result in bacterial resistance and super-infection, prophylactic use is restricted to clinical situations in which benefits outweigh the potential risks. The duration of prophylaxis is dictated by the duration of the risk of the anticipated infection.

4.6 Why are antibiotics important?

Only an effective and timely therapy by a very suitable antibiotic can assuage and cease the infectious diseases which face the population across the globe. Nonetheless, there is not going to be an end for the perseverance and endeavor to overcome this situation, considering the prevalence trend of the disease. More than one third of the world's population is likely infected by bacterial pathogens. Despite the existence of antibiotic therapies, respiratory infections, tuberculosis (TB), and malaria continue to persist as major

public health threats in the 21st century. For instance, one third of the world's population is currently infected with TB and almost 9 million people have active TB disease.

According to the WHO report "Priority Medicines for Europe and the World", infectious diseases rank as the highest total burden of disease worldwide as measured in Disability Adjusted Life Years (DALYs)—31% of the total burden. In fact, infectious diseases were identified as the second leading cause of death in the world, placing second in terms of global mortality rates, 2.47 deaths per 1000 (slightly behind cardiovascular diseases, 2.63 deaths per 1000). In 2004, infectious diseases accounted for more than a quarter of deaths at the global level (26.94%). Approximately 2 million fatalities occur per year from bacterial infections. In particular, pneumonia and diarrheal diseases kill approximately 3.8 million children under 5 each year. (Mossialos et al., 2008) ^[50]

Despite these facts, antibiotics still have an overpowering therapeutic value and are necessary for the treatment of many bacterial pathogens and infectious diseases. Therefore, continuous investment into the search for new agents of antibiotics with novel mechanisms of action (MoA) becomes necessary as resistance spreads and the global burden of infectious diseases continues to surge.

Appropriate use of antibiotic, will definitely reduce the mortality, morbidity, costs, and burden of resistance to antibiotics. ^[51; 52; 53]

4.7 Risk of Antibiotic Use

4.7.1 Adverse drug reactions (ADRs):

An adverse drug reaction (ADR) is a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function ^[54]

The reaction may be a known side effect of the drug or it may be new and previously unrecognized.

4.7.1.1 ADR Vs. an adverse event

- An adverse event is any undesirable event experienced by a patient whilst taking a medicine, regardless of whether or not the medicine is suspected to be related to the event. An example of an adverse event is a patient being hit by a car while on a specific medication.
- An adverse drug reaction is any undesirable experience that has happened to the patient while taking a drug that is suspected to be caused by the drug or drugs. An example of an ADR could be a patient experiencing anaphylaxis shortly after taking the drug.

4.7.1.2. Classification of adverse drug reactions

Adverse drug reactions are frequently classified into six different categories ^[55, 56]. These are:

- **Type A Reactions**

Type A, also known as the augmented reactions are a consequence of magnification of the desired pharmacological action of a drug after the normal therapeutic dose, and are normally dose-dependent. Respiratory depression with opioids or bleeding with warfarin, are perfect examples.

This class may also include those reactions that are not directly associated to the pharmacological effects of the drug. Type (e.g. dry mouth that is associated with tricyclic antidepressants).

- **Type B Reactions**

Type B is also recognized as bizarre reactions are new pharmacologically unexpected reactions of the drug. Reactions of this class are less frequent These are less common, and so may only be discovered for the first time after a drug has already been made available for general use. Examples include anaphylaxis with penicillin or skin rashes with antibiotics

- **Type C Reactions**

Type C, or ‘continuing’ reactions, persist for a relatively long time. For example the osteonecrosis of the jaw with bisphosphonates.

- **Type D Reactions**

Type D which are the “delayed” reactions, become apparent some time after the use of a medicine. The timing of these may make them more difficult to detect.

Leucopenia, which can occur up to six weeks after a dose of lomustine, is a known example of them.

- **Type E Reactions**

Type E, or ‘end-of-use’ reactions, are associated with the withdrawal of a medicine.

An example is insomnia, anxiety and perceptual disturbances following the withdrawal of benzodiazepines.

Table 6. Examples of ADRs associated with antibiotics

Drug	ADRs	Cautions	Contraindications
Aminoglycosides	Ototoxicity , reversible nephrotoxicity ,neuromascular blockade with apnoea	Increase dose interval with renal dysfunction	Pregnancy ,myasthenia gravis
Cephalosporines	allergic reactions, anaphylaxis Nephritis and acute renal failure ,superinfections	Penicillin sensitivity	Cephalosporin sensitivity
Erythromycins	GIT disturbances, reversible cholestatic hepatitis with estolate salt.	Hepatic impairment	Avoid estolate salt in pregnancy and in hepatic disease
Fluoroquinolones	tendinitis and tendon rupture , GIT disturbances ,	Epilepsy , renal or hepatic impairment, pregnancy and breast-feeding	
Penicillines	Allergic reactions, anaphylaxis	History of allergy, renal impairment.	Avoid ampicillin and amoxicillin.
Tetracyclines	Discolouration and deformity in growth teeth , photosensitivity , GIT disturbances ,super infection (candidaisis)	Breast-feeding ; avoid i.v route in hepatic impairment	Pregnancy, renal failure, children under 12 years old.
Sulphonamides	Allergy , agranulocytosis,Stevens-Johnson syndrome , kernicterus in neonates ,thrombocytopenia	Blood counts required, maintain adequate fluid intake.	Pregnancy , infants under 6 weeks, renal or hepatic failure, jaundice, blood disorders
Vancomycin	Ototoxicity , reversible nephrotoxicity, red man syndrome	Avoid extravasations at injection site, renal function test required.	

4.7.2 Drug Interactions:

These can be either kinetic, e.g. enzyme induction or inhibition or dynamic, e.g. two drugs negatively affecting the same organ. Examples include the followings:

1- Aminoglycoside Antibiotics

Aminoglycosides should be avoided during pregnancy because of the high of risk of foetal ototoxicity, therefore concurrent use of other ototoxic drugs, e.g. high ceiling diuretics, minocycline and also concomitant use of nephrotoxic drugs, e.g. amphotericin B, vancomycin, cyclosporine and cisplatin should be highly restricted. Using aminoglycosides in middle aged and patients with kidney failure must be with cautions. ^[57,58]

2- Tetracyclines

Tetracyclines cross the placenta and could be excreted in breast milk. Therefore they should be avoided during pregnancy and lactation. With patients who suffer from renal or hepatic problems tetracyclines should also be given with caution. They may raise blood urea levels, so their co-administration with diuretics should be restricted. They should not be administrated intrathecally. ^[59]

3- Chloramphenicols:

Chloramphenicol interacts with tolbutamide, chlorpropamide, warfarin, cyclophosphamide and phenytoin by inhibiting their metabolism; so toxicity occurrence is most possible if dose adjustments are not done. Failure of therapy may occur with concomitant use with Phenobarbitone, phytoin, rifampin because they increase its concentration. ^[60]

4- Sulfonamides

The co-administration of sulfonamides with phenytoin toblutamide and warfarin leads to the enhancement of the effect of these drugs. This is because it

inhibits their metabolism and it also displaces their protein binding. Sulfonamides interact with methotrexate thus decreasing its renal excretion, therefore toxicity can occur. ^[59]

5- Quinolones

Co-administration of theophylline, caffeine and warfarin with Quinolones mainly ciprofloxacin, norfloxacin and pefloxacin increase their plasma concentration due to inhibition of their metabolism thus toxicity of these drugs may occur. Seizures are reported with non-steroidal anti-inflammatory drugs (NSAIDs). QTc interval prolongation occurs when using quinolones concomitantly with antiarrhythmics (e.g., class IA and III agents). Increased serum digoxin is associated with the use of Gatifloxacin. ^[61]

6- Macrolides

Erythromycin and other macrolides inhibit hepatic oxidation of many drugs resulting in a rise of the plasma levels of theophylline, carbamazepine, valproate, ergotamine and warfarin, where INR should be carefully monitor. Inhibition of CYP3A4 leads to Q-T prolongation; serious ventricular arrhythmias and death have been reported. ^[62]

7- Beta-Lactams

Ceftriaxone IV and IV calcium-containing solutions should not be administered within 5 days of each other to patients aged less than 10 weeks due to the risk of cardiopulmonary adverse events in neonates associated with precipitation of a ceftriaxone-calcium salt in the lung and/or kidneys. But for all other patients, administration should not be within 48 hours.

4.7.3 Superinfections

Drug therapy, particularly with broad spectrum antimicrobials or combinations of agents, can lead to alterations of normal microbial flora of the upper respiratory, intestinal and genitourinary tracts, permitting the overgrowth of opportunistic organisms, especially fungi or resistant bacteria. These infections are often difficult to treat. Superinfection is a common cause of treatment failure and high economic burden. For instance, superinfection caused by *Stenotrophomonas maltophilia* and *Pseudomonas aeruginosa*. Following imipenem therapy, vaginal overgrowth of *Candida* or of resistance staphylococci in the intestinal flora associated with tetracycline. [63; 64]

4.7.4 Antibiotics Resistance

4.7.4.1 What is Antibiotic Resistance?

Antibiotic resistance is a complex process which results from the use and misuse of antibiotics. It is a process by which bacteria changes and develops properties that make the drugs used to treat them ineffective^[50]

Severity of Antibiotic Resistance

Antibiotic resistance has become a day to day challenge of very major magnitude to local, national, and global public health; therefore the possibilities of effectively treating infectious diseases have been substantially reduced because of resistant bacteria.

Furthermore, the risks of complications, morbidity and mortality for patients^[65] have been much increased due to antibiotic resistance. It is well known that the third leading death in the EU is due to infectious diseases^[66]. The problem is further complicated and risks are escalated as resistance to entire antibiotic classes (e.g. β -Lactams, Quinolones, Tetracyclines, Glycopeptides and Macrolides) is also emerging rapidly. (Mossialos et al. 2008)^[50]

Antibiotic resistance trends in developing countries

In developing countries, owing to the fact that antibiotics are available over the counter; which leads to self-medication and inappropriate use of antibiotics, a very high level of resistance has been noticed.

In view of the absence of access to more affordable and effective antibiotics^[67], resistance in developing countries often leads to death.

4.7.4.2 Causes of Antibiotic Resistance:

Following are the two reasons for the cause of growth in antibiotic resistance:

- Related to how antibiotics are used in practice
- Related to insufficient investment in to research for diagnostics and antibiotics

4.7.4.2.1 Reasons related to the use of antibiotics:-

- **Misuse of antibiotics:**

Differences in the consumption and prescribing patterns of antibiotics depends on the incidence of CA infections, cultural and social determinants, pharmaceutical market, regulatory practices, public knowledge about antibiotics and resistance, and the healthcare system, structure and resources. ^[68] Numerous studies confirm that increased antibiotic consumption is associated with the emergence of antibiotic resistance worldwide ^[69]

In order to determine whether or not, policies encouraging reduction of antibiotic consumption can in fact slow the rapid spread of resistance, it is imperative to compare antibiotic consumption trends to rates of antibiotic resistance.

- **Physicians and healthcare providers:**

It is a present day challenge to HCPs (Health care providers) as far antibiotic resistance is concerned.

Limiting the emergence of antibiotic resistance and curtailing its spread by treating effectively infectious diseases is the need of the hour. Inappropriate diagnosis and wrong prescription by the health care professionals for e.g. for very common cold is almost 55% of prescriptions of all antibiotics in the U.S. In the year 2001, in the U.S, it has been documented that unnecessary prescription for upper respiratory tract infections amounts to the above figure of 55%. It warrants a more focused approach by all HCPs ^[70]

- **Negative externality:**

Public health benefits of antibiotic consumption will be very much diminished by the negative externality associated with antibiotics resistance [50]

- **Livestock and agriculture:**

Apart from the inappropriate prescriptions and over-consumption of antibiotics, livestock too, get affected due to the acceleration of antibiotic resistance, since antibiotics are used in live stock for growth promotion and treatment of infection. It is worth noting that more than half of all antibiotics produced globally are used in animals [71]

4.7.4.2.2 Reasons related to the insufficient investment into research.

- **The role of diagnostics in antibiotic resistance:** Improvement on the use of antibiotics as well as reduction in cost and time can be achieved by the proper identification of targeted pathogens with rapid diagnostic tests (RDTs) [72]. Determination of the precise cause of the infection [73] has been hindered due to lack of suitable RDTs for the health care practitioners.

- **The Role of Vaccines in Antibiotic Resistance:** Contribution of vaccines has a tilling effect on the ever growing demand for antibiotics as it has reduced the demand for antibiotics to a greater extent and thus slows the spread of antibiotic resistance.

For example, a US study of >37,000 children, heptavalent pneumococcal vaccine (PCV7) vaccination reduced first-line antibiotic prescriptions by 5.7% and second line by 13.3 %. (Mossialos et al., 2008) [50]

- **Lack of New Antibiotics:** Let alone the misuse of antibiotics and deficiencies of available diagnostic tools, the lack of sufficient development

of new and novel classes of antibiotics challenges current efforts to slow the rise of antibiotic resistance. (Mossialos et al., 2008)^[50]

4.7.4.3 Mechanism of Antibiotics Resistance:

A. Genetic alterations leading to drug resistance

Resistance develops due to the ability of DNA to:

- **Spontaneous mutations of DNA:** An example is the emergence of Rifampin resistant Mycobacterium tuberculosis when Rifampin is used as a single drug)
- **DNA transfer of drug resistance:**

B. Altered expression of proteins in drug-resistant organisms:

Following mechanisms mediate the drug resistance:

- **Modification of target sites:** Good example is Methicillin- resistant S. Aureus.
- **Decreased accumulation:** This might be due to the presence of an efflux system that pumps out the drug (Tetracyclines, Primaquine).
- **Enzymatic inactivation:** The ability to destroy or inactivate the antimicrobial agent also can confer resistance on microorganisms. For example, B-Lactamases destroy many Penicillins and Cephalosporins and an Acetyltransferase can convert Chloramphenicol to an inactive compound.^[74: 75]

4.7.4.4 Cost of Resistance:

Three components are involved in the financial burden on resistance:

A. Direct Medical Costs.

It includes the following:

- i. longer length of hospital stay
- ii. Increased costs within services
- iii. An increase of the expenses that will be paid in the control measures of isolation and infection
- iv. Increased frequency of surgical intervention and other complication.

B. Organizational and Infrastructure Costs.

- I. Maintaining surveillance programmes.
- II. Central reference laboratories

C. Indirect Costs.

Potential loss stemming from morbidity and mortality among those with drug-resistant infections. ^[76]

4.7.4.5 Strategies to overcome antibiotic resistance:

- **WHO Global strategy to overcome antibiotic resistance::**

To contain the antimicrobial resistance, WHO has identified several interventions addressing the message to all the concerns (patients, prescribers, dispensers, health authorities, pharmaceutical manufacturers etc) focusing and targeting ^[77]:

- a. Reduction of prescribing, with particular emphasis on those drugs whose consumption has been shown to correlate strongly with resistance;
- b. Development of new formulations or dosing schedules of those drugs whose pharmacodynamic parameters are better suited to cope with highly resistant strain
- c. Encouraging the use of antibiotics with the maximal capability of bacterial eradication.
- d. Training of prescribers and dispensers.
- e. Developing national drugs policies and guidelines.
- f. Reducing the use of agricultural antibiotics.
- g. Encouraging the development of appropriate new drugs and vaccines.

The Centre for Disease Control and Prevention (CDC):

CDC contributed in overcoming the antibiotic resistance by conducting a campaign to prevent Antimicrobial Resistance, that concluded four recommendations^[78];

- Prevent infection
- Diagnose and treat infection effectively
- Use antimicrobial wisely
- Prevent transmission

Tracking antibiotics resistance in the UAE is very humble, since only few studies had been carried out.^[79, 80, 81, 82] **(Table 7)**

Table 7: Some of the studies concerning antibiotics resistance conducted in UAE

<p>S. Al-Muhairi, et al / Monaldi Arch Chest Dis 2006; 65:1, 13-18 ^[84]</p>	<p>For CAP: <i>Haemophilus influenzae</i> (18.6%) and <i>Streptococcus pneumoniae</i> (10%) For HAP: <i>Pseudomonas.aeruginosa</i> in (50% of HAP).</p>	<p>- Retrospective analysis Of Inpatients with pneumonia in the UAE hospital. -Patients were categorised as having community acquired (CAP) or hospital acquired pneumonia(HAP)</p>	<ul style="list-style-type: none"> • Community Acquired Pneumonia (CAP) makes up (80%) of all pneumonia cases admitted to one of the university hospitals. • Resistance rates (23% of H. influenza isolates were resistant to amoxicillin and 22%) pneumoniae isolates were resistant to penicillin),
<p>Al-Zarouni M,et al / Med Princ Pract. 2008;17(1):32-6 ^[85]</p>	<p>Enterobacteriaceae pathogens (<i>Escherichia coli</i>, <i>Klebsiella pneumoniae</i> and <i>Klebsiella oxytoca</i>)</p>	<p>130 <i>Enterobacteriaceae</i> isolated from different specimen types , Enterobacteriaceae comprising of <i>Escherichia coli</i> (n = 83),<i>Klebsiella pneumoniae</i> (n = 45) and <i>Klebsiella oxytoca</i> (n = 2)</p>	<ul style="list-style-type: none"> • High prevalence of ESBL occurs equally among <i>E. coli</i> and <i>K. pneumoniae</i> isolates. • Amikacin and carbapenems were found to be the most useful drugs for treatment of ESBL infections. • The findings of a carbapenem-resistant ESBL-producing <i>E. coli</i> isolate as well as the occurrence of multidrug resistance are of major concern.
<p>Vincent O. Rotimi et al / Med Microbiol 57 (2008), 881-886; ^[86]</p>	<p><i>Salmonella</i> spp</p>	<p><i>Salmonella</i> spp. Isolated from the stool samples of 407 patients with acute diarrhea in tow hospital , different species been isolated e.g. non-typhoidal <i>Salmonella</i>, <i>S. Typhi</i> , <i>S. Paratyphi</i> (B and C).</p>	<ul style="list-style-type: none"> • The prevalence of ESBL-producing <i>Salmonella</i> was about 17 % , which the higher reported prevalence rates in <i>Salmonella</i> spp.,
<p>Sonnevend A et al, J Med Microbiol 55 (2006), 1533-1538 ^[87]</p>	<p><i>Campylobacter jejuni</i></p>	<p>41 <i>Campylobacter jejuni</i> strains isolated from faecal samples of individual patients</p>	<ul style="list-style-type: none"> • All strains were sensitive to erythromycin • (85.4 %) exhibited resistance to nalidixic acid and ciprofloxacin • Results show that the local incidence of fluoroquinolone resistance among <i>C. jejuni</i> is one of the highest reported worldwide.

4.8 Factors influences use of antibiotics

In order to support the rational use of drugs, it is important to collect information on patterns of drug prescriptions and on factors influencing prescribing decisions. Contributed factors are related to: [83; 84; 85; 86]

- Behavioral characteristics of doctors (Prescribers)
- Behavioral characteristics of patients.
- Laxity in regulation of prescribing and dispensing antibiotics

4.8.1 Behavioral characteristics of doctors (Prescribers):

- **Diagnostic uncertainty:** Sometimes it is difficult to diagnose at the early stages whether an infection is viral or bacterial, especially in cases of upper respiratory tract infections and diarrhea.
- **Patient expectation and demand:** Some patients who had in the past been prescribed antibiotics asked to be given these drugs again. Educated patients also named antibiotics that they wanted. Doctors often yield to patients' demand or expectations for prescribing antibiotics.
- **Fear of poor patient outcome:** occasionally patients are not satisfied with other treatment than antibiotics, so doctors feel they must prescribe the antibiotic to satisfy them.
- **Lack of time due to overcrowding:** Doctors, especially those in public sector do not offer enough time to study the patient's case history, do a proper physical examination or educate them
- **Economical incentive from pharmaceutical companies:**

Newly launched antibiotics were prescribed on the advices and recommendations of medical representatives who present the doctors with conflicting non randomized studies in favor of the antibiotic they are promoting.

- **Over-stock of drugs and near-expiry drugs:**

To use the entire stock before it expires, dispensing doctors prescribe these drugs even though they may not be required by the patient.

4.8.2 Behavioral characteristics of patients:

Patients' misperceptions

Beliefs and confidence of patients that antibiotics are the most effective against all infections, regardless of the reasons for these infections, and their etiology, leading them to often request antibiotics from doctors. ^[87] Lee and co-workers in their study revealed, that, out of 197 families in observational, prospective cohort study, there were 53.0% believed that antibiotics were needed to treat colds ^[88]. Most of the patients, who visited their doctors with acute lower respiratory symptoms, come with expectations that antibiotics will be prescribed for them. These expectations have significant influence on prescribing, even when their doctor judges that antibiotics are not indicated ^[89]. Pshetizky and associates asserted that a short explanation by the family physician to the child's parents about the disease and the probable spontaneous improvement could reduce antibiotics use by 50.0% in children with acute otitis media ^[90]. A study conducted in suburban area near New Jersey came across that parents in the suburban setting were more expected to have inappropriately used antibiotics for their children. Conversely, those in the urban setting were more likely to have been discharged by a physician at one health facility and gone to another physician's office in order to obtain antibiotics for their children ^[91].

Self-medication with antibiotics

The WHO has defined self-medication as the use of drugs to treat self-diagnosed disorders or symptoms, or the intermittent or continued use of a prescribed drug for chronic or recurrent disease or symptoms ^[92]. Self medication with antibiotics is frequently

considered one of the factors contributing to drug resistance ^[93]. A study performed in Turkey on a population that has access to primary healthcare services and a physician, 19.1% were found self-administering antibiotics. ^[94]

A Russian study revealed that 83.6% of nine hundreds families were keeping antibiotics for systemic use in their homes, 86.2% out of them declared that they are using antibiotic without a physician's consultation ^[95].

Patients' adherence

Adherence to the prescribed regimen or treatment is defined as 'the patient's tendency to follow medical advice' ^[96]. Any non-compliance for any reasons like treatment affordability, might leads to withdrawal of medications, and certainly worsening of patient's condition ^[97]. Pechère and co-workers in their multinational study concluded that, there was a poor understanding in 10 of the 11 countries of how non-compliance can increase the potential for resistance development ^[98]. A study conducted in a sample of 509 eligible participants, (individuals prescribed a new antihypertensive monotherapy), of which 118 (23.2%) reported non-compliance with their drug treatment ^[99].

4.8.3 Antibiotics policy

4.8.3.1 What is a national drug policy?

A national drug policy is an obligation to a target and a map-reading for action. It conveys and prioritizes the medium- to long-term purposes set by the government for the pharmaceutical sector, and recognizes the main strategies for achieving them. It provides a frame work within which the activities of the pharmaceutical sector can be synchronized. It covers both the public and the private sectors, and involves all the main actors in the pharmaceutical field. ^[100, 97]

4.8.3.2 Why a national drug policy?

The general objectives of a national drug policy are to ensure:

Access: equitable availability and affordability of essential medicines, including traditional medicine;

Quality: the quality, safety and efficacy of all medicines;

Rational use: the promotion of therapeutically sound and cost-effective use of medicines by health professionals and consumers.

Regarding antibiotic policy the WHO recommendation to the government policies are:

- To stick upon only-prescribing available antimicrobials.
- To ensure that only antimicrobials meeting international standards of quality, safety and efficacy are granted marketing authorization.

4.8.3.3 UAE Antibiotic Policy:

According to the national antibiotics policy and guide to antimicrobial therapy, antimicrobial should only be sold or supplied by prescription of an authorized medical practitioner or dentist. For purpose of rational use, antimicrobials are classified into three groups according to the prescribing levels:

- **Group A:** Antimicrobial for common use, all practitioners may prescribes them (Safe, effective and relatively cheap)

- **Group B:** Restricted, are for prescription by specialists (expensive, toxic and new agents)
- **Group C:** For use in primary health care (same like group A) with some omissions ^[101].

Owing to enormous changes that extended since 1998, when the antibiotics policy of the UAE was published, therefore this policy should be re-formulated and arranged in line with current health requirements and recent evidence-based medicine.

4.9. Newly invented and in the pipeline antibiotic agents:

It is known that antibiotics are the only group of medicinal products which are not primarily targeting the human tissue. During the last few years some new antimicrobial agents been introduced.

1- Aminoglycosides: Neoglycosides.

a. Plazomicin

It was known ACHN 490. It is the First member of the neoglycoside. Plazomicin is resistant to enzymatic inhibition.^[102] It inhibits bacterial protein synthesis and exhibits dose-dependent bactericidal activity. It has a Broad spectrum activity against Gram-negative and Gram-positive bacteria. Due to its lower minimum inhibitory concentration (MIC) it's active against Acinetobacter.^[103] There is no evidence of ototoxicity or nephrotoxicity.^[104]

2- Quinolones

a. NXL 101:

It is primarily an inhibitor of topoisomerase IV. It is used mainly against gram negative bacteria and MRSA. Unfortunately, use of NXL 101 is associated with significant QT prolongation but by time this may be overcome.^[105, 106]

b. Delafloxacin

It is in phase II studies. Delafloxacin is active against *S. aureus* including MRSA. It is suitable for infections in low pH environment such as the skin, vaginal tract, urinary tract and intracellularly within the phagosomes.

c. Nemonoxacin

It is in phase II studies. Nemonoxacin is a non-fluorinated quinolone active against pathogens that cause CAP. [107]

d. ACH 702

It is an isothiazoloquinolone, which is highly active against MRSA including biofilms. ACH 702 is also active against a wide range of Gram-negative bacilli as well as *Mycobacterium tuberculosis*. [108,109]

e. Quinazolidiones

It is active against GyrB "gyrase B gene" and ParE "topoisomerase IV" enzymes. It is mainly against Gram-positive organisms and less so against Gram-negative organisms. [110]

f. Oxazolidinone.

Tedizolid and radezolid are two new oxazolidinone that offer an improvement over linezolid. Tedizolid MICs are lower compared with linezolid for staphylococci, streptococci and enterococci. Tedizolid is active against MRSA that possess the *cfr* gene "cfr gene encodes a methyltransferase". [111]

g. Radezolid.

It achieves higher levels inside macrophages and neutrophils it is useful when applied to persistent infections with intracellular organisms. [111, 112]

h. Sutezolid

It was shown to be superior to linezolid in terms of antimycobacterial activity. [113]

3- New β lactams and monobactams.

a. Ceftaroline:

Ceftaroline is a fifth generation cephalosporin. It is active against MRSA (and also vancomycin resistant *S. aureus*).^[114]

b. Avibactam (NXL 104):

It inhibits β lactamases. It has a Broad spectrum of activity including the KPC enzyme “*Klebsiella pneumoniae* carbapenemase” family. Ceftazidime-avibactam is active against *Pseudomonas* but not ceftaroline-avibactam combination.^[115]

c. Ketolides.

Cethromycin and Solithromycin are two new ketolides in development.

Cethromycin has an orphan drug approval by the FDA for the treatment of bioterrorist threats such as anthrax and plague. Both are highly active against Gram-positive organisms but modestly active against Gram-negative bacteria.^[116]

The main indication of Solithromycin would probably be skin and soft tissue infection and community acquired pneumonia.^[117]

4. Tetracyclines

a. Tigecycline:

It is a broad-spectrum glycylyccline. Tigecycline is not a substrate for drug efflux or the ribosomal protection proteins, mechanisms that lead to resistance to tetracyclines. It is useful in the treatment of mixed infections if *Pseudomonas* infection is excluded as it has no activity against this pathogen.

b. Omadacycline

It is similar to tigecycline in its spectrum but unlike the latter, it is absorbed orally. TP-434 is new compound which shares several properties with omadacycline. It given once daily intravenous (I.V.).^[114]

5. Newer glycopeptides.

a. Telavancin:

It is a newly licensed lipoglycopeptide. Telavancin is used for the treatment of Hospital-Acquired Pneumonia (ATTAIN) trials showed that the cure rates with telavancin was 58.9% compared with 59.5% with vancomycin (95% confidence interval for the difference, -5.6% to 4.3%). In the subset analysis, cure rates were higher with telavancin in patients with monomicrobial *S. aureus* infection although patients with MRSA infection had similar cure rates.^[118]

b. Oritavancin:

It is a synthetic derivative of chloroeremomycin. Oritavancin inhibits transglycosylation by binding to the terminal D-alanyl-d-alanine and also binds to the Pentaglycyl Bridge in the peptidoglycan moiety. It's active against vancomycin-resistant enterococci and VRSA. Oritavancin has long half-life and hence can be administered once daily.^[119]

PRACTICAL PART

5. 1 Study I

Study title

Attitudes towards antibiotics use among banking employees in Sudan, Oman and UAE.

5.1.1 Background

Over –the –counter acquisitions of antibiotics in some countries (e.g. Sudan) are with high frequency due to the lack of laws restricting antibiotic sales or a failure to enforce those laws.

Studies showed that approximately 70.0% of the world’s antibiotics are used in the community. These high rates of using these powerful agents may negatively affect their efficacy and resulting in increasing prevalence of resistance. In 2000, the WHO Report "Overcoming Antimicrobial Resistance" identified three key issues for public involvement: improving access to medical services, reducing unnecessary use of antimicrobial drugs and not sharing medication with other people or keeping part of course for another occasion.^[120]

5.1.2 Objective

The aim of this study is to assess current knowledge, attitudes and behaviour towards antibiotics (ATB) among banking employees.

Specific objectives:

- Measure employees’ attitude towards dispensing and prescribing and pattern of antibiotics use.
- Evaluate parents’ awareness of antibiotics use by their children.
- Determine sources of antibiotics use.

5.1.3 Methods

5.1.3.1 Study design

A Descriptive-cross sectional study was conducted In Sudan, Oman and UAE.

5.1.3.2 Study settings

The study was carried out in several central bank branches in the capitals of the above mentioned countries.

5.1.3.3 Study population

Despite the differences in these regions in terms of the socio-economical status (impact on purchasing power) climate (type of existed diseases), but the selected cohort in all these regions are fully medically insured (particularly in Sudan, where the banking employees are one of the fewest socio-economic groups, who have medical insurance).

Our study population consisted of n=450 banking employees (n=150 each region) who were randomly nominated by the managers of the central banks. Participation was voluntary and verbal consent was obtained after briefing the objectives of the study.

5.1.3.4 Data collection

Data were collected through a structured, pretested, validated, self administrative questionnaire (**Appendix 1**). The questionnaire collected demographic data such as age, gender and level of education of each participant. Respondents were asked, whether they used antibiotics during the past year. In order to help the participants to remember the antibiotics they used, we provided a list of the most common used antibiotics in their countries (**Appendix 2**). Participants, who confirmed their use of antibiotics, were asked why and how they obtained their antibiotics, whether they are storing any antibiotics at home, and if they intended to use them personally or for their children without a Doctor's prescription or advice.

5.1.3.5 Statistical analysis:

Data obtained was entered into a micro computer running the statistical package for social sciences (SPSS version 11.0) software to validate and analyze entries. Descriptive statistics were used to describe socio-demographic characteristics of the respondents. Prevalence of self-medication in the community with antibiotics reported as percentage.

5.1.4 Results:

Out of 450 nominated employees (150 each region) 331 employees participated in the study; the rate of response was 64.6%, 74.0%, 82.0% in Sudan, Oman and UAE respectively.

Respondents' Characteristics:

The mean age of respondents was 34 years. Males represented 66.6% of the participants. 198 (59.8%) of the respondents have children under the age of sixteen. 25% have secondary education, 24.5% have secondary vocational education and the rest representing 50.5% are with university graduation. Demographic data were presented in **Table 8**.

Table 8. Demographic data of respondents

Demographics		Region			Total*
		Sudan (n=97)	Oman (n=111)	UAE (n=123)	
Age	21-30	25	79	37	141
	31-40	38	26	60	124
	41-50	27	5	24	56
	>51	7	1	2	10
Gender	Male	53	81	83	217
	Female	44	30	40	114
Education	Secondary	14	56	13	83
	Secondary Vocational	16	45	20	81
	University	67	10	90	167
Have Children		79	54	65	198

*Total Number of all Respondents = 331

Antibiotic Use:

Out of 97 respondents in Sudan 81 (83.50%), while 52 (46.80%) out of 111 and 92 (74.80%) out of the 123 respondents in Oman and UAE respectively reported antibiotics use during the last year. As shown in **Table 9**.

Within the respondents who have children 83.50%, 66.70% and 67.70% in Sudan, Oman and UAE respectively reported antibiotic use for their children during the past year. As illustrated in **Table 10**.

Antibiotic use without prescription:

Among those who reported antibiotic use there are 49.30% in Sudan, 26.90% in Oman and 47.80% in the UAE who used antibiotics without prescription for themselves. As shown in **Table 9**.

Within all parents who reported antibiotics use for their children, 20 (13.70%) of them reported use of antibiotics without prescription for their children in the past year. It is noticeable that this practice is affected by the parents' educational level. As shown in **Table 10**.

Table 9. Antibiotic use among adults

Region	Sudan	Oman	UAE	Total
Total sample	97	111	123	331
respondents reported Antibiotic	81 (83.50%)	52 (46.80%)	92 (74.80%)	225
respondents reported Antibiotic use without prescription**	40 (49.30%)	14 (26.90%)	44 (47.80%)	98

**Note: The percentage of Antibiotic use in each region is calculated from the total number of respondents in that specific region (e.g. % of Antibiotic use in Sudan (83.50%) is calculated from n=97 (100%))*

*** Note: The percentage of antibiotic use without prescription in each region is calculated from the number of respondents who reported the antibiotic use in that specific region (e.g. % of antibiotic use without prescription in Sudan (49.3%) is calculated from n=81 (100%))*

Table 10. Antibiotic use among children

Region		Sudan	Oman	UAE	
Have children		79	54	65	
Reported antibiotic use for children		66	36	44	
Reported antibiotic use without prescription for children		14(21.20%)	3 (8.30%)	3 (6.80%)	
Educational level	Reported antibiotic use without prescription for children	Secondary	1	1	-
		Secondary vocational	-	2	-
		University	13	-	3

Note: the percentage of those who reported antibiotic use for their children without prescription in each region is calculated from the total number of respondents who reported antibiotic use in that region (% of parents reported antibiotic use for their children in UAE (6.8% is calculated from total number of those who reported antibiotic use for their children in UAE n=44)

Antibiotics commonly used:

For the respondents and their children the most frequent antibiotic used was Amoxicillin (40.90% and 46.60% respectively). This was followed by Amoxicillin/clavulanic acid (45%, 29%). However Tetracyclin was used by children under sixteen only with prescription (2.70%) for acne, while adult respondents used Tetracycline with and without prescription (12%). The frequencies of antibiotics commonly used were presented in **Table 11**

Table 11 Commonly used antibiotics among respondents and their children

Used Antibiotics	Frequency of use by respondents*		
	With prescription (n=127)	Without prescription (n=98)	Total (n=225)**
Amoxicilin	55 (59.80%)	37 (40.20%)	92 (40.90%)
Amoxicillin/clavulanic acid	24 (53.30%)	21 (46.70%)	45 (20%)
Ampiclox	22 (66.60%)	11 (33.40%)	33 (14.70%)
Tetracyclin	10 (37%)	17 (63%)	27 (12%)
Cotrimoxazole (Septrin)	5 (55.60%)	4 (44.40%)	9 (4%)
Erythromycin	7 (58.30%)	5 (41.70%)	12 (5.30%)
Norfloxacin	4 (57.10%)	3 (42.90%)	7 (3.10%)
Used Antibiotics	Frequency of use by children*		
	With prescription	Without prescription (n=20)	Total (n=146)**
Amoxicilin	57 (83.8%)	11 (16.20%)	68 (46.60%)
Amoxicillin/clavulanic acid	25 (86.2%)	4 (13.80%)	29 (19.90%)
Ampiclox	19 (86.4%)	3 (13.60%)	22 (15.10%)
Cotrimoxazole	5 (71.4%)	2 (28.60%)	7 (4.80%)
Erythromycin	8 (100%)	0	8 (5.50%)
Cephalxine	8 (100%)	0	8(5.50%)
Tetracylin	4 (100%)	0	4 (2.70%)

**Note: percentage of each used antibiotic with or without prescription is calculated from the total number of respondents who reported the use of this specific antibiotic. (e.g. % of with prescription use of Amoxicillin (59.8%) is calculated from the total Amoxicillin use n=92)*

***Note: The percentage of the total use of each antibiotic is calculated from the total number of respondents who reported antibiotic use. (e.g. % of Amoxicillin use 40.9% is calculated from the total number of people who reported antibiotic use n=225)*

Reason for self medication with Antibiotics:

Respiratory tract infections were reported as the leading reason for antibiotic use with or without prescription for both the respondents and their children. Reasons for which antibiotics by respondents and their children were used are illustrated in **Figures 1 and 2.**

Figure 1. Reasons for antibiotics use by respondents

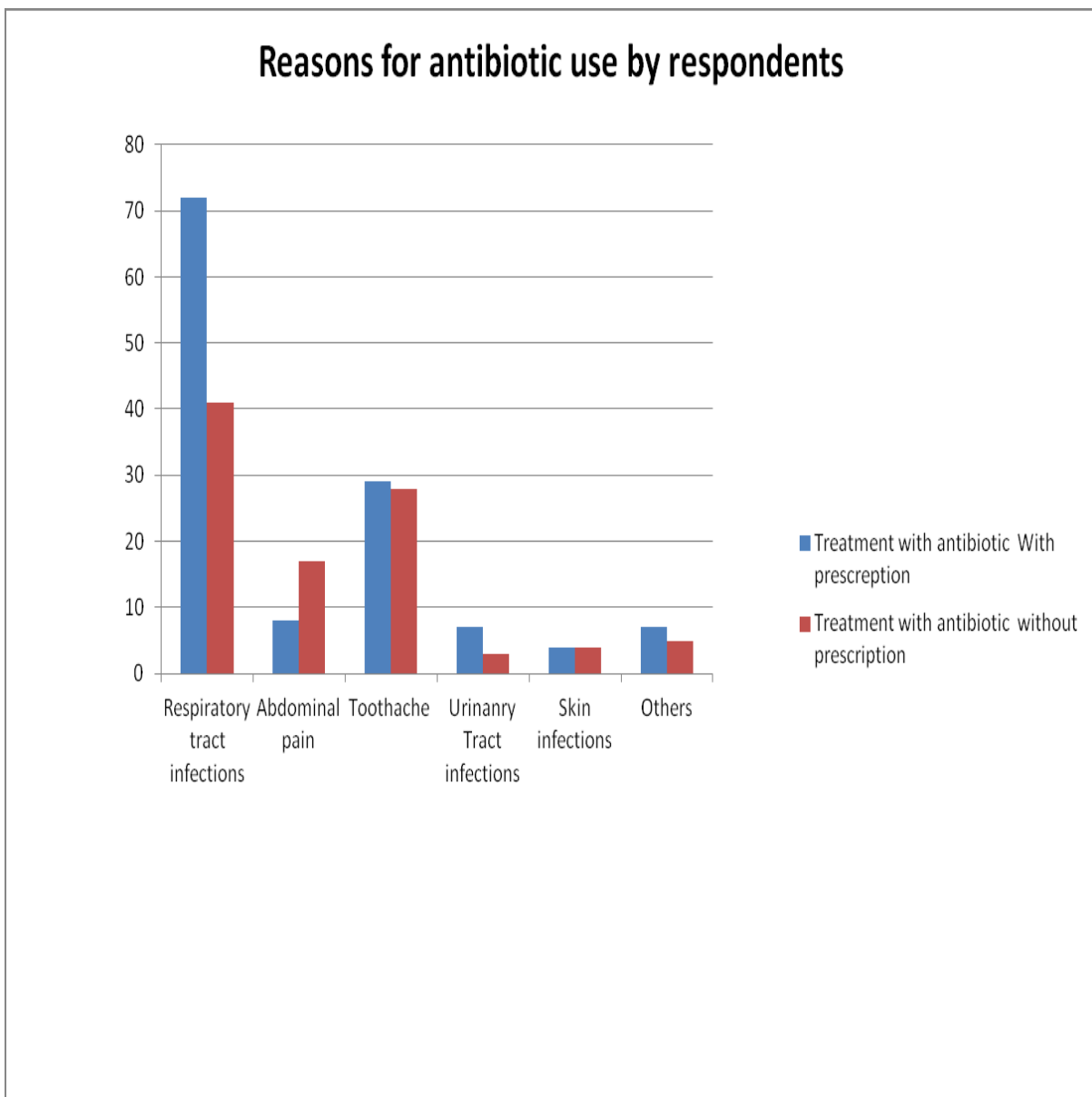
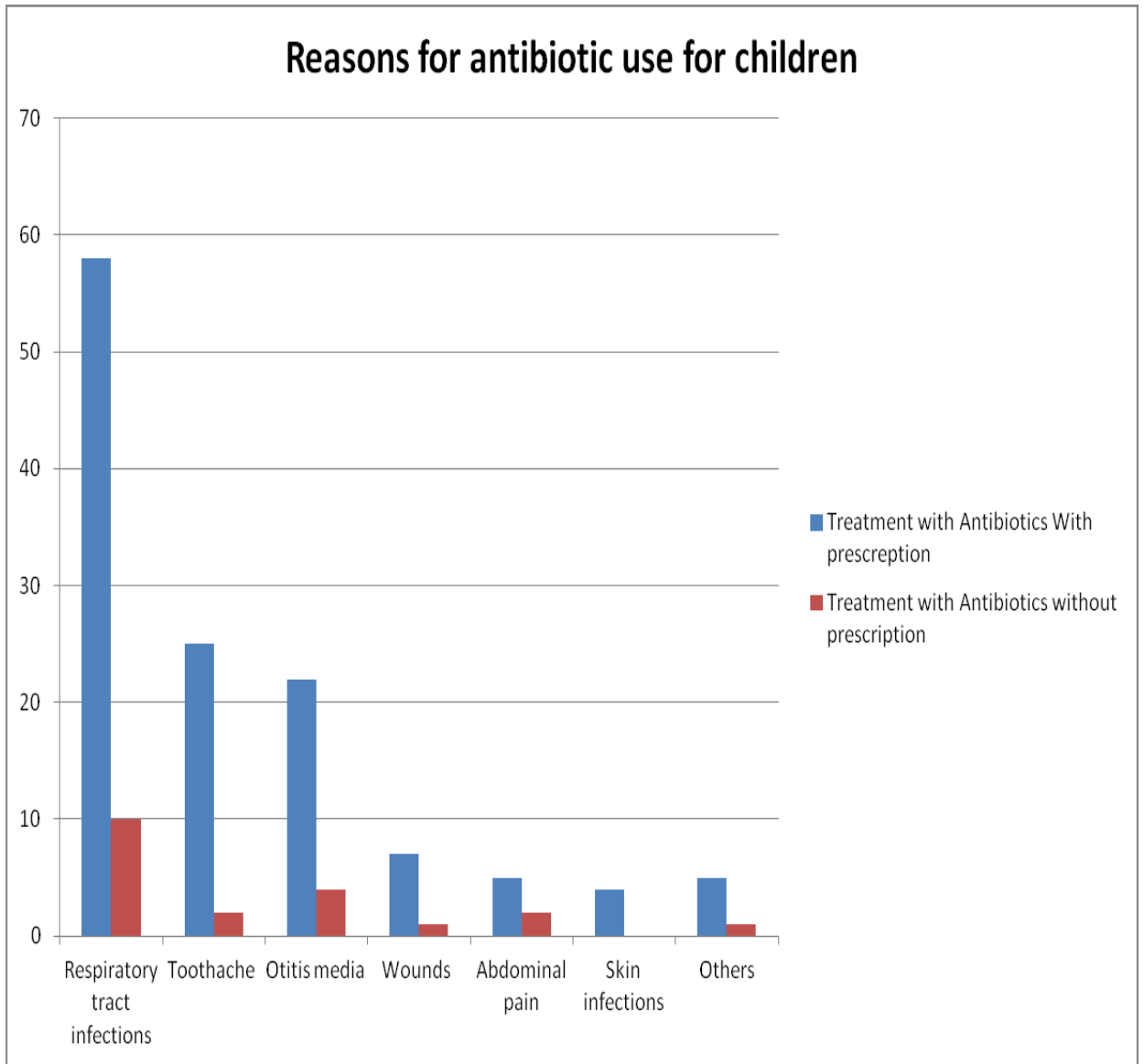


Figure2. Reasons for antibiotic use for children



Source of antibiotics obtained without prescription:

Within those who have used antibiotics without prescription (n=98), 5.1% used the antibiotics based on friends' advices; 24.5% had their antibiotics from leftovers from previous illnesses. Pharmacists' dispenses according to the respondents' complains shared by 17.3% of the non-prescribed acquisition of the antibiotics. 53.1% obtained antibiotics as over the counter based on their own request for the specific antibiotic. As presented in **Table 12**. It is obviously noticeable that the use of antibiotics without prescriptions was to a great extent limited in Oman. This is mainly due to the restricted implementation of the laws that regulate the antibiotic use.

Table 12. Sources of antibiotics obtained without prescription

Source	Sudan n= 40	Oman n= 14	UAE n=44	Total n=98
Friend's advice	2 (5%)	1 (7.10%)	2 (4.50%)	5 (5.10%)
Leftovers from previous prescriptions	10 (25%)	5 (35.70%)	9 (20.50%)	24 (24.50%)
Pharmacist advice according to respondent's complain	7 (17.50%)	2 (14.30%)	8 (18.20%)	17 (17.30%)
OTC based on the respondents request	21 (52.50%)	6 (42.90%)	25 (56.80%)	52 (53.10%)

Note: the percentage of the source of obtained antibiotics without prescription is calculated from the total number of respondents who reported antibiotic use without prescription in each region. (e.g. % of OTC acquisition I Sudan (52.5%) is calculated from the total number of respondents in Sudan who reported antibiotic use without prescription (n=40)).

5.1.5 Discussion:

Miss use and overuse of antibiotics beside the emergence of resistance bacteria have also resulted in enormous expenditures and adverse drug reactions. In both developed and developing countries, many factors have been reported with the overuse and misuse of antibiotics including drug use policies, economics, prescribers' knowledge, patients' expectations, inaccurate diagnoses and pharmaceutical market.

The selected cohort in these regions are fully medically insured (particularly in Sudan, where the banking employees are one of the fewest socio-economic groups who have medical insurance).

In our study we assessed the banking employees' demographic profile in terms of their age, gender, educational level and whether they have children below sixteen years old or not with regard to their attitude towards antibiotics and if, they used them with or without prescription. The study was conducted through a structured, pretested, validated, self-administrative questionnaire, which has some differences with other questionnaire of similar objectives in Europe ^[121] to be harmonized with the intra-cultural conditions in these regions. The questionnaire has contributed to a relatively low response rate (73.6%) in comparison with studies conducted in US (87%) ^[122] and Turkey (100%) ^[123]

The study participants was composed of 33.4% female while the female participation rate in a Sudanese and Nepalese studies, was 54.9% and 28% respectively. ^[122, 124]

The prevalence of self medication with antibiotics within our study group is rated 43.56% which is higher than what have been reported in Turkey and Spain 32.2% and 32.1% respectively. ^[123, 125] But it much lower that what been reported from Lithuania (53.2%). ^[126]

The most frequently used antibiotics in our study with or without prescriptions are Amoxicillin, Amoxicillin/clavulanic acid combination, Ampiclox, Cotrimoxazole, Erythromycin and Tetracylin, in descending order. This pattern was almost similar to those from Croatia, Russia, Sudan and Trinidad and Tobago.^[127, 128, 124, 129]

Study results showed that, healthcare providers prescribing antibiotics for respiratory infections, which were most likely viral in origin. Such a prescription pattern will likely contribute to the emergence and spread of resistance. Like many studies.^[130, 131] Erythromycin which is known to be extensively metabolized by cytochrome P-450 3A (CYP3A) isozymes, and its concomitant use with the medication that inhibits the effects of CYP3A may increase its plasma concentration, that can cause ventricular arrhythmias and sudden death, been reported as self-medicated and prescribed antibiotics^[132, 133], which is most probably used with some of these agents like, Ketoconazole, Miconazole, (fungal infection are more frequent in UAE and Oman due to humid weather) quinine the drug of choice for malaria in Sudan), and Co-trimoxazole.

Through all over the globe dispensing antibiotics is subjected to prescriptions but still the problem of self-medication with antibiotics is not exclusively in developing countries but it is also common in the developed countries.

Acquisition of antibiotics without prescription used to be through different ways like friends' advice, over the counter, leftovers from previous prescriptions without consulting a healthcare provider. This practice was reported by 24.5% of our study sample which is remarkably similar to a US study results (26%).^[134]

Similar to other studies conducted in Sudan, Russia and Trinidad and Tobago our results revealed that the most frequent indications and reasons for self-medication with antibiotics were as follows: acute respiratory tract infections, toothache, intestinal disorders, urinary tract infections and others. ^[124, 128, 135]

5.1.6 Limitations of the study:

Respondents have been selected by the managers according to the availability of the staff at the period in which the study was conducted, which may affect a proper sampling selection. Despite we provided a list of the common marketed antibiotics in these regions respondents found difficulties in recalling and remembering the antibiotics they have used.

5.1.7 Conclusion:

Self-medication with antibiotics is reasonably high within banking employees in Sudan, Oman and UAE. Multi factorial interventions are believed to reduce the incidence of this practice including: an intensive public health plans; awareness regarding the consequences of self-medication with antibiotics throughout health education and restrictions that stop the availability of antibiotics without prescription.

5.2 Study II

Self-medication with antibiotics by the community of Abu Dhabi Emirate, United Arab Emirates (UAE)

5.2.1 Introduction

Efforts to promote the rational use of drugs have been targeted mainly at the formal health care services. This started back in 1970s, when the World Health Organization (WHO) introduced the concept of essential drugs. The principle of this concept is that a limited number of drugs would lead to better supply of drugs, better prescribing and lower costs for health care. Despite the introduction of the essential drug list in some 110 countries at present, drug consumption increased worldwide ^[136]. It could be argued that antibiotics have done more to improve public health in the last 50 years than any other measure, however; it is estimated that the worldwide market of antibiotics consumes between 100 and 200 x 10⁶ kg of products which products ^[137]. Differences in implementing drug regulations that affect the availability of antibiotics in different countries can play an important role in misconceptions about antibiotics ^[138].

Self-medication can be defined as the use of drugs to treat self-diagnosed disorders or symptoms, or the intermittent or continued use of prescribed drugs for chronic or recurrent disease or symptoms (Awad et al, 2005; WHO, 2000) ^[124, 139]. A literature review emphasizes that there were no published studies in UAE that addressed self medication with antibiotics by the community, which places the current study to be one of the rare published data in this field.

Survey results in Europe showed significant differences in public attitudes, beliefs and levels of knowledge concerning use of antibiotics, self-medication and antibiotics resistance ^[138].

Overall, only half of the respondents in the survey were aware about antibiotic resistance. This awareness was the lowest in countries with higher a prevalence of resistance ^[139].

In Spain for instance, common self-medication with antibiotics might be a consequence of poor implementation of and control over the laws and regulations influencing prescribing and influences community pharmacy services even more ^[140].

Many practitioners, veterinarians, breeders, farmers and analysts work on the assumption that antibiotics undergo spontaneous degradation. It is well documented that the indiscriminate use of antibiotics has led to water contamination, selection and dissemination of antibiotic-resistant organisms and alteration of the fragile ecology of the microbial ecosystems. The damages caused by the overuse of antibiotics include hospital, waterborne and food borne infections by resistant bacteria, enteropathy (irritable bowel syndrome, antibiotic-associated diarrhea etc.), drug hypersensitivity, biosphere alteration, and destruction of fragile inter-specific competition in microbial ecosystems ^[141]. The consequences are severe. Infections caused by resistant bacteria fail to respond to treatment, resulting in prolonged illness and greater risk of death. Treatment failures also lead to longer periods of infectivity, which increase the numbers of infected people moving in the community and thus expose the general population to the risk of contracting resistant strains of infection ^[142].

United Arab Emirates (UAE) is a federation of seven gulf emirates with estimated population of 4.1 million people of different ethnic groups (79.9 % are expatriates) ^[143]. The gross national product per capita (GNP) is \$32000 ^[144]. Standards of health care in the UAE are

generally high, reflecting the high level of public spending over the decades since the oil boom. Better health provision has been reflected in rapidly improving figures for key indicators such as life expectancy and infant mortality rates, which are now at western levels [143]. According to the national antibiotics policy and guide to antimicrobial therapy, antimicrobial should only be sold or supplied on prescription of an authorized medical practitioner. For purpose of rational use, antimicrobials are classified into three groups according to the prescribing levels [101].

5.2.2 Objectives

The aim of the study was to estimate the prevalence of self medication with antibiotics in Abu Dhabi.

5.2.3 Methods

A Descriptive-cross sectional study was conducted during Abu Dhabi Book Fair; in April 2006. Written approval to conduct the study was obtained from the Health Authority of Abu Dhabi (HAAD) (**Appendix 3**),

5.2.3.1 Setting

The study was conducted during the Book Fair days in April 2006, which is annually take place in the Cultural Foundation that located in the heart of Abu Dhabi city, the capital of the United Arab Emirates .Cultural Foundation is a national independent authority, was created to meet the needs of the cultural and civilization in the state to promote the spread of culture and plays an essential role in cultural development as an important part of the overall national development.

5.2.3.2 Study population and sample size

The visitors of the Book Fair were invited to participate in the study; verbal consent was obtained after briefing the objectives of the study. Selection of the participants was based on a systematic random sampling. Every 35th visitor was chosen.

5.2.3.3 Data collection

Data were collected through a structured, pretested, validated, self administrative questionnaire (**Appendix 1**). The questionnaire collected demographic data such as age, gender and level of education of each participant. Respondents were asked, whether they used antibiotics during the past year. In order to help the participants to remember the antibiotics they used, we developed a portrait containing labels from the available types of antibiotics in the health premises as shown in **Appendix 4**. Participants, who confirmed their use of antibiotics, were asked why and how they obtained their antibiotics, whether they are storing any antibiotics at home, and if they intended to use them personally or for their children without a Doctor's prescription or advice.

5.2.3.4 Statistical analysis

Data obtained was entered into a micro computer running the statistical package for social sciences (SPSS version 11.0) software to validate and analyze entries. Descriptive statistics were used to describe socio-demographic characteristics of the respondents. Prevalence of self-medication in the community with antibiotics reported as percentage. P value was calculated by setting the reference value and comparing it with other values. $P < 0.05$ was considered statistically significant.

5.2.4 Results

Out of 1000 invited visitors 860 agreed to participate in the study; the rate of response was 86.0%. Males represented 65.8% of the participants, while females represented 34.2%. The age and educational levels were presented in **Table 13**. Among 860 participants, 485 (56.3%) reported antibiotics use during the last year (68.5% of them were males and 31.5 % females). There were no significant associations between gender and use of antibiotics use. However; use of antibiotics was significantly affected by age $p < 0.001$ as well as the educational level ($p=0.023$). The frequencies of antibiotics commonly used were presented in **Table 14**. Amoxicillin was the antibiotic most commonly used by the participants and for their children (46.3% and 70%’ respectively), it was followed by amoxicillin/clavulanic acid combination (23.9%, 10.8%). However, ciprofloxacin and norfloxacin were used only by adult participants and not used for their children.

Table 13. **Distribution of demographics characteristics within the study population**

Respondents' characteristics	Distribution of total No. of respondent $n = 860$ (%)	Distribution of respondent reported antibiotic use $n = 485$ (%)
<u>Gender</u>		
Male	566 (65.8%)	332 (68.5%)
Female	294 (34.2 %)	153 (31.5 %)
<u>Age</u>		
20 – 29	238 (27.7 %)	100 (20.6 %)
30 - 39	331 (38.5 %)	176 (36.3 %)
40 – 49	222 (25.8 %)	159 (32.8 %)
50>	69 (8.0%)	50 (10.3 %)
<u>Education</u>		
Primary	173 (20.1%)	80 (16.5%)
Secondary	191 (22.2 %)	112 (23.1%)
University & Postgraduates	496 (57.7 %)	293 (60.4%)

Antibiotic use wasn't associated with nor the gender neither the educational level of the respondents (p value = 0.134 and p value = 0.023 respectively). Antibiotic use was significantly associated with the respondents' age.

Table 14. Frequencies of used antibiotics

No	Name of ATB	No. of used courses by adults <i>n</i> =485(%)	No. of used courses by children <i>n</i> =360 (%)
1	Amoxicillin	226 (46.6%)	252 (70%)
2	Amoxicillin/clavulanic acid	116 (23.9%)	39 (10.8%)
3	Erythromycin	14 (2.9%)	10 (2.8 %)
4	Tetracycline	31 (6.4%)	7 (1.9%)
5	Clarithomycin	12 (2.5%)	4 (1.1%)
6	Azithromycin	31 (6.4%)	19 (5.3%)
7	Ciprofloxacin	4 (0.8%)	-
8	Cotrimoxazole	15(3.1%)	6 (1.7%)
9	Norfloxacin	20 (4.1%)	-
10	Cefuroxime	10 (2.1%)	13 (3.6%)
11	Cefixime	6 (1.2%)	5 (1.4 %)
12	Cefaclor	-	5 (1.4%)

Within those who have used antibiotics, there were (n=485, 55.7%) obtained their antibiotics with a prescription either from a physician or a dentist, while the remaining (44.3%) acquired their antibiotics without a prescription as self-medication (**Table 15**). The results have showed that method of obtaining antibiotics was significantly affected by the age of the participants ($p = 0.014$). Among parents who confirmed their use of antibiotics for their children (n= 360), results revealed that 65.5% have received antibiotics through a prescription and 34.4% without a prescription. (**Table15**)

Table 15. Sources of obtaining antibiotics

Source	Adults n=485(%)	Children n=360 (%)
Physician	222(45.8%)	195(54.2%)
Dentist	48(9.9%)	40(11.1%)
OTC from Community pharmacy	140(28.9%)	89(24.7%)
OTC from abroad	56(11.5%)	28(7.8%)
Left over	19(3.9%)	8 (2.2%)

The most common reasons for which antibiotics were used were illustrated in **Table 16**.

Table 16. Frequencies of common reasons for which antibiotics were used:

Reason	Adults n=485(%)	Children n=360 (%)
Influenza	157(32.4%)	159(44.2%)
General infection	119(24.4%)	66(18.3%)
Toothache	60(12.4%)	61(16.9%)
Upper respiratory	32(6.6%)	14(3.9%)
Gastrointestinal	26(5.4%)	12(3.3%)
Ear infection	11(2.3%)	27(7.5%)
Genitor-urinary	36(7.4%)	-
Others	44 (9.1%)	21(5.8%)

There were (n= 393, 45.6%) out all participants stated that, they can intentionally uses antibiotics as self-medication without a medical consultation, which was significantly affected by the educational level of the visitors ($p < 0.001$). There were (n= 245, 28.5%) out of all participants declared that they were keeping antibiotics at home, which they have mostly acquired from the community pharmacies without a prescription (**Table17**). A significant association was found between the behavior of keeping antibiotics at home, gender (n= 151 males; $p < 0.001$) and age ($p=0.002$).

Table 17. Demographics of Respondents Keeping Antibiotics at home:

Respondents' characteristics	Antibiotics home with prescription n =8 (%)	Antibiotics home without prescription n =237 (%)
<u>Gender</u>		
Male	0(0%)	151(63.70%)
Female	8(100%)	86(36.30%)
<u>Age</u>		
20 – 29	5 (62.50%)	33 (13.90%)
30 - 39	1 (12.50%)	89 (37.60 %)
40 – 49	1 (12.50%)	91 (38.40 %)
50>	1 (12.50%)	24 (10.10 %)
<u>Education</u>		
Primary	2(25%)	32 (13.50%)
Secondary	0 (0 %)	45 (18.90%)
University & Postgraduates	6 (75 %)	160(67.50%)

The tendency of keeping antibiotics at home is significantly associated with the age and gender of the respondents '(pvalue=0.001andpvalue=0.002 respectively).

5.2.5 Discussions

This study represents the first published work on irrational antibiotic use through self medication with antibiotics at a community level in Abu Dhabi (capital city of the United Arab Emirates) and conducted by a cross-sectional study that included a large number of the Abu Dhabi's Book Fair visitors who sampled based on a systematic random sampling. Every 35th visitor was chosen.

Despite the UAE's declared antimicrobial policy that restricts dispensing of antibiotics without prescription, our study indicated the availability of these agents over the counter. This has revealed the high prevalence of self-medication with antibiotics in the studied population. The rate of use of antibiotics (56.3%) was fairly high as compared with results conducted in Czech Republic (31.1%), Jordan (23.0%) and Lithuania (39.9%) [145, 146, 147]. In Lithuania, women tended to use more antibiotics than men. Our results have showed that the use of antibiotics was not associated with gender, however; it was significantly affected by age ($p < 0.001$) and well as educational level ($p=0.023$). The high prevalence of self-medication that was found within the adult participants (44.3%) and their children (34.4%) might be anticipated due to the nature of UAE community, which comprises different nationalities (79% are expatriates) [143]. The majority being from India, Philippines, Pakistan, Europeans and different Arab countries, where the prevalence of self-medication was also high. For instance, the self-medication with antibiotics was, (48.1%) in Sudan and (39.5%) in Jordan and (18%) in India [124, 146, 148]. This confirms that traditional, social and cultural factors influence the self-medication with antibiotics, despite being prescription only medicine in UAE. Furthermore, this high prevalence might also be attributed to the easy acquisition of antibiotics from the community pharmacies. Another reason that might be entailed is the lack of disciplinary

regulations in antimicrobial policies in UAE. Regarding the reported results from studies in Sudan, Jordan and Greece India [124; 146; 149], amoxicillin was the most preferably chosen antibiotic even as self medication. Other antibiotics that were used included, amoxicillin /clavulanic acid combination , macrolidies, quinilones and tetracyclines. As stated by the participants in the current study, influenza had been the major reason that mostly treated by prescribed or self -medication antibiotics. This finding, though consistent with results from other studies [146, 147; 150], also confirms the belief of the community that antibiotics can treat and eradicate any infection irrespective of their origin .It also revealed that the participant were unaware of the consequences of inappropriate use of antibiotics. Despite its highly harming photosensitivity, our results revealed the inappropriate and irrational use of tetracyclines in treating gastrointestinal problems a practice which is in accordance with some published guidelines which state the drug is to be used mostly in a combinations with other medicines to manage food borne illnesses caused by different types of bacteria (Brucella abortus, Vibrio cholerae, Vibrio vulnificus) [151] or for initial H. pylori treatment failure regimen (salvage therapy) [152, 153]. Despite its highly harming photosensitivity, our results revealed the inappropriate and irrational use of tetracycline in treating gastrointestinal problems. This is a practice which is in discordance with published guidelines, which state the drug is to be used in combination with other medicines to manage food-borne illnesses caused by various bacteria (e.g. Brucella abortus, Vibrio cholera and Vibrio vulnificus) [151] or following initial H. pylori treatment failure (salvage therapy) .

Intended self-medication and storage of antibiotics at home were both considered to be predictors of actual self-medication, as reported by Grigogyan and colleagues [121]. Comparing our results with those reported from Malta and Czech Republic (22.0%, 7.5% respectively),

we found that the main source of obtaining these antibiotics were the local community pharmacies. Our study also revealed that retrieving medications from abroad was another common source, especially those which were expensive (100% of home stored azithromycin in our study were brought from outside the UAE). Participants also declared that another important reason for storing antibiotics at home was their ineligibility for medical insurance benefits.

5.2.6 Study limitations

The limitation to the current study was related to the sampling of the population. Since our sample was drawn from attendees in a book fair. These book-fair visitors were generally intellectual and educated. Therefore the sample might not cover the different groups representing the diverse Abu Dhabi -UAE society.

5.2.7 Conclusions

The results of the study confirmed that antibiotic self-medication is a relatively frequent problem in UAE. Interventions at different levels are required in order to reduce the frequency of antibiotics misuse. Quick and co-workers ^[154] classified these interventions into managerial, regulatory, educational and financial. Managerial interventions: involve work on up-dating the antibiotics policy and Guide to Antimicrobial therapy 2nd Edition 1998, establish a National Antibiotic Therapeutic Advisory Committee, and establish National Standard Treatment Guidelines. Regulatory strategies involve limiting the import of drugs to the market ^[135]. The educational interventions for both prescribers (flow charts, newsletters, bulletins and others) and patients/consumers (educational campaigns on antibiotics, their uses and limitations) are of paramount importance. With regards the financial intervention: The National mandatory health insurance scheme may play an important role to diminish this problem.

5.3 Study III

A comparative study between prescribed and over –the-counter antibiotics

5.3.1 Introduction

United Arab Emirates (UAE) consists of seven Emirates. Abu Dhabi emirate is the largest Emirate, which lies on a T-shaped island jutting into the Arabian Gulf from the central western coast with an area of 67,340 km² and estimated 1.85 million population. In 2001 General Abu Dhabi Health Service (GAHS) was established; this oversee the running of all Abu Dhabi's hospitals and primary health centers. GAHS also regulate the private health institutes, including the pharmacy sector which is composed of community pharmacies and pharmaceutical ware houses. In the year 2007 GAHS was replaced by two organizations namely; the regulatory body named the Health Authority of Abu Dhabi (HAAD) and an operational body named Abu Dhabi Health Services Company (SEHA). The pharmacy practice and pharmacies in Abu Dhabi Emirate were regulated according to the UAE Federal Law entitled: Article No. 4 (1983) for pharmaceutical profession.

The alarming global increase in microorganisms resistant to antibiotics poses a major public health problem. Although the increasing resistance can be attributed to several factors, a major cause is the overall volume of antibiotics consumption. Other contributory factors were, wrong diagnosis, indiscriminate prescribing and dispensing errors ^[155]. The professional activities of the community pharmacists have changed completely in arrears to the increasing number of available pharmaceuticals including many antibiotics. In addition to assuring high quality in dispensing, responsibilities of the pharmacists have been extended to include detection, prevention, and resolution of drug-related problems ^[155]. Several studies related to the quality of dispensing antibiotics, have been conducted. Pharmacists' social demographic, educational

background ^[156, 157] and opinion about their activity have been considered as the most likely determinants of the quality of dispensing ^[158, 159]. In recent years, one study on antibiotics prescribing concluded that small doses and long duration were both associated with increased risk of antibiotic resistance. ^[160] Antibiotics consumption should be reduced to avoid and diminish its serious environmental impacts. There are several studies focusing on the disproportionate excessive use of antibiotics ^[161, 162]. Setting a proper antibiotic policies and raising the community awareness of the danger behind inappropriate use of antibiotics may contribute in diminishing the problem. Promoting the appropriate use of antibiotics through various interventions will help to avoid unwarranted prescribing and misuse of antibiotics ^[155]. For appropriate interventions to be carried out across the community, it is important to know to what extent the population uses antimicrobials. Enhanced surveillance could play a positive role in controlling antimicrobial over-use or misuse. Countries such as Denmark and Spain have a database of antibiotics prescribed for all patients in the country. Prescription information for various populations (e.g., children versus adults) and between different provinces of the country have been analyzed to determine trends in antimicrobial use at the population level ^[163, 164]. OTC dispensing of antibiotics is common especially in developing countries.

In UAE it's illegal to dispense an antibiotic without a prescription, therefore we conducted this study to know to how extend the pharmacists adhere to the laws and Regulations.

5.3.2 Objectives

The main objectives of this study were:

1. To examine the influence of demographic characteristics (age, gender and years of work experience) of the pharmacist with respect to dispensing antibiotics (with and / or without prescription) in terms of legalization, rationality and safety.

2. To examine the pattern of dispensing antibiotics (with and / or without prescription) in terms of frequency, costs and indications (reasons for dispensing).

5.3.3 Methods

5.3.3.1 Study Design

This was a cross-sectional study, was conducted in Abu Dhabi Emirate, the capital of UAE,. Written approval to conduct the study was obtained from Health Authority of Abu Dhabi (HAAD), UAE. (**Appendix 5**).

The study was conducted during the study period from March to September 2009.

5.3.3.2 Study Settings

The allocation of the study sites was accomplished based on the pharmacies geographical area in Abu Dhabi city. The study carried out in (n= 24) randomly selected community pharmacies out of (n= 240) located in Abu Dhabi city during the study period from March to September 2009. The random selection was performed by means of sealed envelope technique and was accomplished by a third party details. Each 10 pharmacies were represented by one pharmacy, based on the geographical location of pharmacies in Abu Dhabi Emirate. Pharmacies included in the study were identified from the MoH pharmacy database in the federal

government located in Abu Dhabi capital and serving the whole UAE. The final list of selected pharmacies was allocated from the HAAD the regulatory body in Abu Dhabi Emirate.

5.3.3.3 Sample size

The World Health Organization (WHO) manual ^[165] recommended that 600 encounters [20 facilities and 30 (patients or prescriptions) per facility] were sufficient to reflect the power of the study and the statistical inferences. We used a multistage cluster sampling (pharmacies represented the cluster and pharmacists represented the population), assuming that there were more than one pharmacist in the pharmacy; therefore each pharmacy was represented by one pharmacist. This yields (n= 24) pharmacists for the target population. The purpose of the study has been explained to the selected consenting pharmacists by a structured information sheet. The confidentiality of the information was maintained. **(Appendix 6) (Appendix 7)**

5.3.3.4 Data collection

The data included information about the dispensed antibiotics [trade name, generic name, strength and duration of treatment]. The study of the pattern of dispensing antibiotics (with and/or without prescription) in terms of, frequency, costs and indications (reasons for dispensing) was permitted via the administration of questionnaire. Pharmacists were asked to complete their demographic data and to collect the required data from patients' dispensed antibiotics (with or without prescriptions). The data was collected during the study period, irrespective of completion of the 100 encounters for all transactions dealt, with antibiotics with or without prescription.

V. The questionnaire

We developed a closed-structured questionnaire **(Appendix 8)** to examine the influence of demographic characteristics (age, gender and years of experience in pharmacy practice) of

each pharmacist with respect to dispensing antibiotics (with and/or without prescription) in terms of legalization, rationality and safety.

Questionnaire content

Data collection booklet consisted of four sections:

- Pharmacist's sociodemographic data (age, gender and years of experience in pharmacy practice)
- Consumer's sociodemographic data (age, gender, socioeconomic status)
- Dispensed antibiotic's data (trade name, generic name, strength, duration of treatment, cost, and mode of dispensing (with or without prescription))
- The reasons for dispensed antibiotics (the indication for using the antibiotics by consumers)

The financial status of patients were determined using a scale ranging from low monthly income (≤ 2000 Arab Emirates Dirham's-AED), medium monthly income (>2000 AED and < 5000) and high monthly income (≥ 5000 AED) based on each individual monthly income.

Questionnaire administration

The questionnaire was administered by the represented pharmacist ($n= 24$) in each of the cluster sample in the 24 pharmacies. Pharmacists were asked to complete their demographic data in each section and to fill the required data from the individual consumer (both with and without prescription). Each pharmacist was required to fill the data relevant to ($n= 100$) individual pharmacy visitors (consumers).

5.3.3.5 Statistical analysis

All data were entered, and analyzed by using SPSS version 17. Descriptive statistics were generated to determine patterns of antibiotics distribution. Variables found in the univariate analysis with significance at the 0.05 or higher (e.g. pharmacist code, age, gender and years of experience in pharmacy practice, –consumer gender and socio-economic status consumer) were all strained into a multivariate model. Forward stepwise logistic regression was used .Odds ratios (OR), significance, and 95% confidence intervals (95% CI) were calculated to predict the related factors of dispensing antibiotics with or without prescription.

5.3.4 Results

Of the 24 selected pharmacies, only 20 pharmacists completed the questionnaire; at a response rate of 80%. Demographic characteristics of the participating pharmacists were shown in **Table 18.**

Table 18: Demographic Characteristics of the pharmacists (n=20)

Age:	
26—30	3 (15%)
31— 40	8 (40%)
41—51	9 (45%)
Gender:	
Male	10 (50%)
Female	10 (50%)
Years of work experience:	
4—5	2 (10%)
6—10	4(20%)
11—20	11(55%)
21—26	3(15%)

Participating pharmacists dealt with a total of (n= 1645) patient's transactions involving antibiotics, which were dispensed either with prescriptions [n=1211, (73.6%)] or without prescriptions [n=434, (26.4%)]. Only one pharmacist did not dispense antibiotics without a prescription during the study period. Results have shown highly significant associations between pharmacists' age ($p=0.001$) and gender ($p=0.001$) and practice of dispensing antibiotics. The male pharmacists had preponderance over the female pharmacists in dealing with antibiotics dispensed as OTC. There was an increase in antibiotics dispensed without prescriptions associated with the years of pharmacists' experience in pharmacy practice. Over 61.0% of the study population was between 31-50 years of age (patients and consumers). Gender and socioeconomic status have significantly affected the manner in acquiring antibiotics without a prescription ($p=0.012$ and $p=0.001$); respectively. The males and participants with low socioeconomic status tend to request antibiotics without a prescription more frequently. Patients and consumers demographics were shown in **Table 19**.

Table 19: Patient / Consumer characteristics:

variable	individuals <i>n</i> =1645	with prescription <i>n</i> = 1211	without prescription <i>n</i> = 434
Age			
17 – 28	484 (29.40%)	360 (29.70%)	124 (28.60 %)
29 – 40	635 (38.60%)	446 (36.80%)	189 (43.50%)
41 – 52	375 (22.80%)	306 (25.30%)	69 (15.90%)
> 52	151 (9.20%)	99 (8.20%)	52 (12.00%)
Gender			
Male	949 (57.7%)	717 (59.2%)	232 (53.5%)
Female	696 (42.3%)	494 (40.8%)	202 (46.5%)
Socio-Economic Status			
High	314 (19.1 %)	237 (19.6%)	77 (17.7%)
Medium	949 (57.7%)	768 (63.4%)	181 (41.7%)
Low	382 (23.2%)	206 (17.0%)	176 (40.6%)

**The socio-economic status and the gender of the respondents are significantly associated with the practice of using antibiotics without a prescription. (p value= 0.001 and p value= 0.012 respectively)*

Logistic-regression model have yielded the following strong predictors for dispensing antibiotics without a prescription: pharmacist's age (OR= 1.36; $p=0.001$), pharmacist's gender (OR 0.621; $p=0.001$), years of pharmacists' experience in pharmacy practice (OR 0.686; $p=0.001$), patient's socioeconomic (OR 1.836; $p=0.001$) and patient's gender (OR, 1.346; $p=0.012$). The results were shown in **Table 20**.

Table 20. Logistic Regression model for factors associated with dispensing and acquiring antibiotic without Prescription

Variable	P value	Odd Ratio	95% CI*	
			Lower	Upper
Pharmacist age	0.000	1.357	1.178	1.564
Pharmacist gender	0.000	0.621	0.476	0.811
Pharmacist experience	0.000	0.686	0.593	0.793
Patient-customer age	0.515	1.004	0.992	1.016
Patient-customer gender	0.012	1.346	1.067	1.698
Patient-customer Socio Economic	0.000	1.836	1.532	2.201
Reason	0.880	1.002	0.979	1.025

*CI: Confidence Interval

The probability of dispensing antibiotics without a prescription increased as the age of pharmacists' increases too. Furthermore, male consumers with low socioeconomic status increased the likelihood of acquiring an antibiotic without a prescription. We did not identify any relationship between patient's age, reason (diagnosis/symptoms) and acquiring an antibiotic without a prescription.

Types of antibiotics used.

Over the study period, 25 types of antibiotics were dispensed with and without a prescription. Mann-Whitney U test showed a significant difference between antibiotics dispensed with a prescription and those without ($p < 0.001$). Clarithromycin, cefuroxime and amoxicillin/clavulanic acid were the most dispensed antibiotics with a prescription (91.5%, 91.3%, and 66.4%, respectively). Ceftriaxone, amoxicillin and amoxicillin/clavulanic acid were the most frequently dispensed antibiotics without a prescription (53.3%, 47.8%, and 33.6%, respectively). Antibiotics such as ofloxacin, moxifloxacin, cefprozil, cefixime, cefidininir and spiramycin were dispensed with prescriptions, while cotrimoxazole and spectinomycin were dispensed without a prescription. (**Table 21**). Antibiotics dispensed with a prescription were used for treatment duration of 5, 7 and 10 days, while those dispensed without a prescription were used for 3 to 7 days. The treatment duration mean of prescribed antibiotics was 6.47 ± 2.62 days. The treatment duration mean of antibiotics dispensed without prescription was 5.74 ± 2.484 days. The differences between the two treatment durations (antibiotics dispensed with prescription and antibiotics dispensed without prescription) was statistically significant ($p < 0.000$).

Each dispensed antibiotics was stratified according to Anatomical Therapeutic Chemical Classification (ATC). The trend was expressed by the J01 (third level of ATC system). The total

cost for each subgroup is presented in **Table 22**. The total retail cost of all dispensed antibiotics was 152,112 Arab Emirates Dirham's AED (41,560 United States Dollars USD). Those dispensed with a prescription totaled 122,961 AED (33,595 USD); 80.8% of total cost. Those dispensed without prescription totaled 28,151 AED (7,691 USD); 19.2% of total cost. The therapeutic subgroup (J01C) was the leading subgroup, with a total cost of 46,435 AED (12,687 USD) on prescription antibiotics, and 13,804 AED (3,771 USD) on antibiotics dispensed without a prescription (29.7%). The macrolide subgroup (J01F) yielded a total cost of 36,088 AED (9,860 USD)

Table 21. Frequencies and rank of dispensed antibiotics

Code	Generic name	ATC	Total of transaction	Frequency of dispensing				Rank in Total transaction
				With prescription		Without prescription		
				No. of transaction	%	No. of transaction	%	
1	Amoxicillin/clavulanic acid	J01CR02	402	267	66.4%	135	33.6%	1
2	Clarithromycin	J01FA09	235	214	91.1%	21	8.9%	2
3	Amoxicillin	J01CA04	212	99	46.7%	113	53.3%	3
4	Cefuroxime	J01DC02	183	167	91.3%	16	8.7%	4
5	Ciprofloxacin	J01MA02	140	110	78.6%	30	21.4%	5
6	Azithromycin	J01FA10	109	79	72.5%	30	27.5%	6
7	Ceftriaxone	J01DD04	69	36	52.2%	33	47.8%	7
8	Moxifloxacin	J01MA14	53	53	100%	0	0%	8
9	Cefdinir	J01DD15	35	35	100%	0	0%	9
10	Cefixime	J01DD08	27	27	100%	0	0%	10
11	Ampicillin	J01CA01	25	13	52%	12	48%	11
12	Cefpodoxime	J01DD13	22	17	77.3%	5	22.7%	12
13	Levofloxacin	J01MA12	21	16	76.2%	5	23.8%	13
14	Metronidazole	P01AB01	19	6	31.6%	13	68.4%	14
15	Metronidazole	P01AB01	19	6	31.6%	13	68.4%	14
16	Metronidazole	J01XD01	16	12	75%	4	25%	15
17	Norfloxacin	J01MA06	16	14	87.5%	2	12.5%	15
18	Clindamycin	J01FF01	14	11	78.6%	3	21.4%	16
19	Ofloxacin	J01MA01	6	6	100%	0	0%	17
20	Spiramycine	J01FA02	5	5	100%	0	0%	18
21	Co-trimoxazole	J01EE01	5	0	0%	5	100%	18
22	Erythromycin	J01FA01	4	1	25%	3	75%	19
23	Cefprozil	J01DC10	4	4	100%	0	0%	19
24	Clotrimazole	G01AF02	3	3	100%	0	0%	20
25	Spectinomycin	J01XX04	1	0	0%	1	100%	21
Total			n=1645(100%)					

Table 22. Distribution of J01 Antibiotic and cost

ATC	Name of therapeutic subgroup	Cost		Total cost
		With prescription	Without prescription	
J01A	Tetracyclines	1002	205	1207
J01C	Penicillins	32631	13804	46435
J01D	Other beta-lactam antibacterials	36786	5504	42290
J01F	Macrolides	31634	4454	36088
J01M	Quinolones	20616	4904	25520
J01E	Sulphonamides & Trimethoprim	0	205	205
J01X	Other	292	75	367
Total		122961	29151	152112

**Cost in Arab Emirates Dirham, 1\$ = 3.67 AED*

Reasons for prescribing and dispensing antibiotics

The study results revealed that the most prescribed and OTC dispensed antibiotic was Co-amoxiclav for several reasons (**Table 23**). Amoxicillin/clavulanic acid was prescribed for sore throat where as it was dispensed more as an OTC this is also the case with amoxicillin. Coamoxiclav was preferred over cefuroxime and clarithromycin, while azithromycin was more likely to be chosen by the pharmacists. The results indicated that coamoxiclav and cefuroxime were frequently prescribed for cough, whereas amoxicillin and Amoxicillin/clavulanic acid were favoured as OTC. Amoxicillin/clavulanic acid and clarithromycin were prescribed as well as dispensed as OTC for common cold. Amoxicillin/clavulanic acid, cefuroxime, clarithromycin, and azithromycin were the most prescribed antibiotics for upper respiratory tract infection, whereas amoxicillin, amoxicillin/clavulanic acid and azithromycin were dispensed as OTC. Cefixime and Moxifloxacin were not dispensed as OTC, but were always dispensed with prescription for upper and lower respiratory tract infections. Results revealed that Ceftriaxone was similarly prescribed by doctors and dispensed without prescription for sexually transmitted diseases (STD). Ciprofloxacin was the most widely prescribed antibiotic for urinary tract infections. Amoxicillin and macrolides (clarithromycin and azithromycin) were usually prescribed and dispensed as OTC for infection with *Helicobacter. Pylori*. Dentists and pharmacists have both favoured amoxicillin and amoxicillin/clavulanic acid for dental infections.

Table23. Reasons of Dispensed Antibiotics

No.	Generic name	Reasons for dispensing																																	
		With Prescription														OTC Dispensing																			
		Sorethr Throat	Fever	Sinusitis	Cough	Tonsillitis	Bronchitis	Influenza	Otitis Media	Diarrhea	H.pylori	UTI	STD	Acne	Wounds Injuries	Toothache	Others	Sorethr Throat	Fever	Sinusitis	Cough	Tonsillitis	Bronchitis	Influenza	Otitis Media	Diarrhea	H.pylori	UTI	STD	Acne	Wounds Injuries	Toothache	Others		
1	Amoxicillin	8	10	3	2	2	4	2	4	4	22				4	35	5	26		11	2	1	19								1	57			
2	Co-amoxiclav	38	47	23	33	42	23	14	8			1		16	58		45	33	2	22	19	2	22	1						4	34				
3	Cefuroxime	31	44	9	41	37	48	2	1			5	2	2				3		2	2	9													
4	Ceftriaxone	1		4		2	10						36															33							
5	Cefixime	4	9	1	1	6	4	4				7																							
6	Cefdinir	3	1		3	5	5					7																							
7	Clarithromycin	33	27	19	26	9	54	11			47	3						4	4	9	4	3	2												
8	Azithromycin	8	12	6	19	7	22					5		1				12	11	3	6	6	3												
9	Ciprofloxacin	3	12	3		3	8		3	3		43						2			1	1													
10	Moxifloxacin	2	10	10	2	4	8		8																										

5.3.6 Discussions

In the current study we assessed pharmacist's socio demographic profile in terms of their age, gender and years of work experience with regard to dispensing antibiotics with or without prescription. This was conducted through a closed-structured questionnaire. This has contributed to the relatively high response rate of the selected sample of pharmacies (80%) as compared to (98.8%) rate which have been reported from Spain ^[166] and 37.7% reported previously in the UAE ^[167]. The gender of participating pharmacists was equally distributed, when compared to the gender of participants in a Pakistani study ^[168] in which they were predominantly males (99%).

The results revealed a significant association between the pharmacist's age and the rate of dispensing antibiotics without a prescription ($p=0.001$). Also In addition, 95% of the pharmacists in the study dispensed antibiotics without a prescription, which has exceeded the 85% rate reported in Brazil ^[169]. During the study period a total of 1645 transactions involving antibiotics were reported; 73.6% with a prescription from a physician or dentist and 26.4% without a prescription. The reported results were better than those reported in Jordan (42.5%), Nigeria (57.7%), Mongolia (57.9%), and Palestine (60%), respectively. ^[170, 171, 172, 173]

The males within the consumers cohort, (57.7%) were and more likely to acquire antibiotic without a prescription, especially, those with a low socioeconomic status.

The logistic regression model results have indicated that the risk factors associated with antibiotics dispensed without prescription were pharmacist's age, gender and years of work experience, as well as patient socioeconomic status and gender. Similar findings have been reported in Spain ^[166], Jordan ^[145] and Brazil. ^[174]

Regarding specific antibiotics, results have revealed that, the top ten dispensed antibiotics in descending order were amoxicillin/clavulanic acid, clarithromycin, amoxicillin, cefuroxime, ciprofloxacin, azithromycin, ceftriaxone, moxifloxacin, cefdinir and cefixime,. This pattern was similar to that reported from Croatia, ^[175] yet differs from those reported in Indonesia ^[176] where widely- restricted amphenicols (chloramphenicol group) are still in use despite their harmful aplastic anemia side effect. Healthcare providers continue prescribing antibiotics for respiratory infections, which were most likely viral in origin. Such a prescription pattern will likely contribute to the emergence and spread of resistance. ^[177, 178]

The most common reason for both dispensing antibiotics with prescription and dispensing antibiotics without a prescription was upper respiratory tract infections. These infections were mostly non-specific type in which sinus, pharyngeal and lower airways symptoms were frequently presented but no compelling evidence for bacterial infection. It has been reported that pharmacists can have the same behavior of physicians in prescribing broad spectrum antibiotics ^[179] due to their experience to perform quick and simple examination on the patient with symptoms of respiratory infections.

Another reason for this behavior may be due to the persistent requests from patients from the pharmacist to dispense antibiotics to them without a prescription according to their previous treatment experiences and avoiding the extra charges when consulting a physician.

Although the major cause of urinary tract infection was *Escherichia coli*, which was resistant to quinolones and fluoroquinolones, ^[180, 181] the current study results revealed that both prescribers and dispensing pharmacists were still recommending them. Furthermore, no

patient in the studied population was treated by the drug of choice, nitrofurantoin, which was a compelling indication for the infection by this pathogen. ^[182]

Prevalence of dispensing antibiotics without a prescription in Abu Dhabi has declined since the implementation of a mandatory medical insurance program by HAAD. This decline has reached 68.4% in 2005. ^[167, 15]

Our data showed a further decline of 26.4%, nearly half the rate reported in 2006. This can be attributed to the insurance mandate, since patients must now acquire a prescription for the needed antibiotic. The enforcement of the mandate requires that the offending pharmacist will be suspended from practice for 30 days, therefore; few pharmacists were dispensing antibiotics without prescriptions. Furthermore, HAAD is now a member of The Alliance for the Prudent Use of Antibiotics (APUA). HAAD is organizing workshops on antibiotics overuse, antibiotics resistance and a campaign to raise the adherence of pharmacists to the antibiotics mandate.

The study findings revealed that, there was a lack of antibiotic usage guidelines, which was anticipated to lead to antibiotics misuse and over-prescribing, as in accordance with other similar studies. ^[166, 167, 174]

Antimicrobial resistance is a worldwide threat affecting both industrialized and developing countries. ^[183]

Controlling the use of antibiotics is of paramount importance in both the community and hospital settings. The first step to overcome this is by identifying the prescribing, dispensing and consumption of the antibiotics used in the community. ^[184]

Therefore, we believe that in order to combat the problem of OTC dispensing of antibiotics, it is necessary to enhance pharmacists and patients awareness, perform random surveillance and legislate and impose rules and regulations on antibiotics dispensing as well as prescribing.

5.3.7 Limitation of the study

We have utilized self-administrated questionnaire by participating pharmacists to collect data; however, this method of data collection may experienced the following Limitations: 1) it may raise some discrepancies within the participating pharmacists with different work load 2) it may also increase the chances that the questionnaires been filled by the pharmacy technician.

5.3.8 Conclusions

Prevalence of dispensing antibiotics by community pharmacists without prescription is illegal and alarming. Pharmacists with long pharmacy practice dispense antibiotics as OTC more often than younger ones. Pharmacists and patients' perception, knowledge and attitude are crucial in developing interventions to improve the current practices of dispensing antibiotics. Insurance company may develop low-priced formulary antibiotics models to help low income patients to acquire their antibiotics after consulting the physicians. It's recommended to avail

antibiotics, such as Nitrofurantion for UTIs as an alternative to the Quinolones in order to reduce resistance to Ciprofloxacin also drug utilization research have become critical, in order to gain firsthand knowledge of what is being consumed. In the absence of this research, and subsequent guidelines, protocols and policies, it would not be possible to identify the problems and set priorities to improve and change current practice. Further research and patient interviews will provide greater insight into the problem.

6. Abstract:

Charles University in Prague, Faculty of Pharmacy in Hradec Kralove

Department: Department of Social and Clinical Pharmacy

Candidate PharmDr. Abobakr Abasaeed Elhag

Supervisor : prof. RNDr. Jiri Vlcek, CSc.

Title of Doctoral Thesis: Analysis of the Use of Antibiotics in the United Arab Emirates

Introduction and Aims:

The misuse of antibiotics for viral infections (for which they are of no value) and the immoderate use of broad spectrum antibiotics instead of narrower spectrum antibiotics have been well-documented and reported. Therefore the inappropriate use of antibiotics is getting a global problem, mainly in the developing countries. Emergence of antibiotics resistance is often a result of irrational prescribing patterns, misuse of the antibiotics as well as self-medication.

Although the United Arab Emirates (UAE) antimicrobial policy restricts dispensing of antibiotics without prescription, studies revealed the wide availability of these agents over the counter (OTC), their over prescribing pattern and the high prevalence of self-medication with antibiotics, unfortunately and regardless of this results, there is a lack and paucity in studies that tracking the prevalence of antibiotics resistance. The aim of our research was to evaluate the attitude of the community towards the use of antibiotics, estimate the prevalence of self-medication with them, identify the socio-demographic factors, which are related to the community and the pharmacists, that affecting this practice. In our research we also identify the frequent used antibiotics, their sources of obtaining and the reasons why they used.

1. Attitudes towards antibiotics use among banking employees in Sudan, Oman and UAE.

Aims:

The aim was to assess current knowledge, attitudes and behaviour towards antibiotics (ATB) among banking employees, evaluate parents' awareness of antibiotics use by their children and determine sources of antibiotics use.

Methodology:

A descriptive-cross sectional study was conducted in Sudan, Oman and UAE, targeted banking employees. A 18-item questionnaire was used for data collection. Descriptive statistical analysis was done in SPSS® version 11 software.

Results:

450 employees were nominated (150 each region), only 331 employees participated in the study; the rate of response was 64.6%, 74.0%, 82.0% in Sudan, Oman and UAE respectively. Mean age was 34 years. Males represented 66.6%. Within the participants 49.3%, 26.9%, and 47.8% were reported antibiotics use without prescription in Sudan, Oman and UAE respectively. Parents with higher educational level were tending to give their children antibiotics without prescription mainly in Sudan. Amoxicillin and amoxicillin / clavulanic acid were the leading used antibiotics by respondents and their children mainly for respiratory tract infections. 53.1% obtained antibiotics as over the counter based on their own request for the specific antibiotic.

Conclusion:

Self-medication with antibiotics is reasonably high within banking employees in Sudan, Oman and UAE. Multi factorial interventions are believed to reduce the incidence of this practice including: an intensive public health plans; awareness regarding the consequences of self-medication with antibiotics throughout health education and restrictions that stop the availability of antibiotics without prescription.

2- Self-medication with antibiotics by the community of Abu Dhabi Emirate, United Arab

Emirates (UAE)

Aims:

The study aimed at identifying the major socio-economic factors that are related to self-medication with antibiotics and the main types of antibiotics used in this practice and reasons behind it. Another goal was to characterize the sources of obtaining antibiotics without prescription.

Methodology:

A Descriptive-cross sectional study was conducted during Abu Dhabi Book Fair; in April 2006. Visitors of the Book Fair were invited to participate in the study. Data were collected through a structured, pretested, validated, self administrative questionnaire. In order to help the participants to remember the antibiotics they used, we developed a portrait containing labels from the available types of antibiotics in the health premises.

Data obtained was entered into a micro computer running the statistical package for social sciences (SPSS version 11.0) software. P value was calculated by setting the reference value and comparing it with other values. $P < 0.05$ was considered statistically significant.

Results:

Out of 1000 invited visitors 860 agreed to participate in the study; the rate of response was 86.0%. Males represented 65.8% of the participants. Use of antibiotics was significantly affected by age $p < 0.001$ as well as the educational level $p=0.023$. Amoxicillin was the antibiotic most commonly used by the participants and for their children (46.3% and 70% respectively). 44.3% acquired their antibiotics without a prescription as self-medication. The method of obtaining antibiotics was significantly affected by the age of the participants $p= 0.014$. There were 45.6% out all participants stated that, they can intentionally use antibiotics as self-medication without a medical consultation, which was significantly affected

by the educational level of the visitors $p < 0.001$. A significant association was found between the behavior of keeping antibiotics at home and the gender

$P < 0.001$ and age $p=0.002$. Influenza had been the major reason that mostly treated by prescribed or self-medication antibiotics. This finding confirms the belief of the community that antibiotics can treat and eradicate any infection irrespective of their origin.

Conclusion:

The study confirmed that antibiotic self-medication is a relatively frequent problem in UAE. Interventions at different levels are required in order to reduce the frequency of antibiotics misuse. Managerial interventions: involve work on up-dating the antibiotics policy and guide to antimicrobial therapy 2nd Edition 1998, establish a National Antibiotic therapeutic adviser committee. The educational interventions for both prescribers and patients/consumers (educational campaigns on antibiotics, their uses and limitations) are of paramount importance. Moreover, the National mandatory health insurance scheme may play an important role to diminish this problem.

3- A comparative study between prescribed and over –the-counter antibiotics

Aims:

The main aims of this study were to examine the influence of demographic characteristics (age, gender and years of work experience) of the pharmacist with respect to dispensing antibiotics (with and / or without prescription) in terms of legalization, rationality and safety and to examine the pattern of dispensing antibiotics (with and / or without prescription) in terms of frequency, costs and indications (reasons for dispensing).

Methodology:

Cross-sectional study, conducted in Abu Dhabi Emirate during the period from March to September 2009. The study carried out in (n= 24) randomly selected community pharmacies. Data were collected through closed-structured questionnaire. The cost was calculated in Emirate Dirham, each dirham is equivalent to 3.7 US\$. Data were entered and analyzed using SSPS version 17. Descriptive Statistics: odds ratios (OR), significance and 95% CI were calculated and logistic regression was conducted.

Results:

Participating pharmacists conducted a total of 1645 transactions involving antibiotics, 1211 (73.6%) dispensed with prescriptions and 434 (26.4%) without prescriptions. Strong predictors for dispensing antibiotics without a prescription using the logistic-regression model were pharmacist's age ([OR] 1.36; P=.001), pharmacist's gender (OR 0.621; P=.001), experience (OR 0.686; P=.001), and patient's socioeconomic (OR 1.836; P=.001) patient's gender (OR, 1.346; P=.012) Clarithromycin, cefuroxime and amoxicillin/clavulanic acid were the most frequently dispensed antibiotics with a prescription (91.5%, 91.3%, and 66.4%, respectively). Ceftriaxone, amoxicillin and amoxicillin/clavulanic acid were the most frequently dispensed antibiotics without a prescription (53.3%, 47.8%, and 33.6% respectively). Antibiotics

dispensed with a prescription were frequently given as a 5-, 7- or 10-day regimen, while those dispensed without a prescription were frequently given for duration of 3 to 7 days. Co-amoxiclav was commonly dispensed for sore throat without a prescription. Ceftriaxone was dispensed at a similar rate, both with and without a prescription for sexually transmitted diseases (STD).

Conclusion:

Prevalence of dispensing antibiotics by community pharmacists without prescription is illegal and alarming. Pharmacists with long pharmacy practice dispense antibiotics as OTC more often than younger ones. Pharmacists and patients' perception, knowledge and attitude are crucial in developing interventions to improve the current practices of dispensing antibiotics. Insurance company may develop low-priced formulary antibiotics models to help low income patients to acquire their antibiotics after consulting the physicians. Drug utilization research have become critical, in order to gain firsthand knowledge of what is being consumed.

7. Abstrakt

Univerzita Karlova v Praze, Farmaceutická fakulta v Hradci Králové, katedra sociální a klinické farmacie

doktorand PharmDr. Abobakr Abasaeed Elhag

Školitel : prof. RNDr. Jiri Vlcek, CSc.

Název disertační práce: Analýza používání antibiotik ve Spojených arabských emirátech.

Úvod a cíl:

Zneužívání protiinfekčních léčiv pro léčbu virových infekcí a masivní preference širokospektrých antibiotik před úzko-spektrými je dobře dokumentována a publikována. Proto nevhodné užití antibiotik se stává globálním problémem, především v rozvojových zemích. Antibiotická rezistence může vznikat i v důsledku neracionálního užití léčiv, zneužívání antibiotik stejně jako samoléčení antibiotiky.

Ačkoli Spojené Arabské Emiráty (UAE) zakazují výdej antibiotik bez předpisu, studie ukazují snadnou dostupnost těchto léčiv k samoléčení a rozsáhlé zkušenosti se samoléčením v regionu a při tom nejsou zde dostupné informace o vývoje rezistence. Cílem naší studie bylo popsat vztah populace k užívání antibiotik, určit prevalenci samoléčby a identifikovat sociodemografické faktory, které charakterizují populaci či lékárníky pozitivně nakloněných k samoléčbě antibiotiky. V naší studii bylo prvním cílem sledovat jaká antibiotika jsou nejčastěji k samoléčbě využívána, jaký byl jejich zdroj a důvod k použití. Práce měla následující projekty:

1. Analýza používání antibiotik mezi bankovními úředníky Sudánu, Ománu a UAE

Cíle:

Analyzovat současné znalosti, postoje a chování k antibiotikům (ATB) mezi bankovními úředníky a určit zdroje antibiotické spotřeby

Metodika:

Deskriptivní průřezová studie byla provedena v Sudanu, Omanu a nebo UAE na populaci bankovních úředníků. Byl použit 18-ti položkový dotazník. Deskriptivní analýza byla provedena pomocí statistického software SPSS® verze 11.

Výsledky:

450 respondentů bylo požádáno o účast ve výzkumu (z každé země 150). 331 souhlasilo s svou účastí ve studii a proto návratnost byla 64.6% v Súdánu, 74.0% v Ománu a 82.0% v UAE.

Průměrný věk respondentů byl 34 let. Většinu souboru tvořili muži (66.6%). V Súdánu užívalo antibiotika 49.3%, v Ománu 26.9%, a v UAE 47.8% respondentů. Především v Súdánu měli rodiče s vyšším vzděláním tendenci častěji užívat antibiotika k samoléčbě svých dětí.

Amoxicillin a potenciální amoxicillin byly preferenčními přípravky používaných při samoléčení jak respondenty tak i jejich dětí. Antibiotika byla nejčastěji používána pro léčbu respiračních nemocí. 53.1% respondentů požadovalo v lékárně konkrétní antibiotikum a ne radu jak léčit jejich potíže.

Závěr:

Samoléčba antibiotiky je vysoká mezi bankovními úředníky všech tří zemí – Súdánu, Ománu a UAE. K redukci této praxe je nutné hledat komplexní řešení včetně intenzivní zdravotní politiky, vymezení role samoléčení a zdůrazňování jejich rizik a restriktivní opatření s cílem snížit dostupnost antibiotik bez předpisu.

2- Samoléčba antibiotiky u občanů emirátu Abu Dhabi Spojených arabských emirátů (UAE)
Cíle:

Cílem studie je identifikovat základní socio-ekonomické faktory ovlivňující samoléčbu antibiotiky a identifikovat která antibiotika jsou takto používána a proč.

Jiným cílem je charakterizovat zdroje, kde lze získat antibiotika bez předpisu

Metodologie:

Deskriptivní průřezová studie byla realizována mezi účastníky knižního veletrhu v Abu Dhabi v dubnu 2006. Data byla získána strukturovaným, validovaným dotazníkem, který respondent vyplnili sami. Pro připomenutí jména přípravku byl vyroben náhled balení jednotlivých dostupných antibiotik.

Data byla hodnocena pomocí statistického software SPSS (verze 11.0).

Výsledky:

860 z 1000 oslovených návštěvníků souhlasilo s účastí ve studii (návratnost je 86.0%). Muži reprezentovali 65.8% respondentů. Používání antibiotik signifikantně ovlivnil věk ($p < 0.001$) a stupeň dosaženého vzdělání ($p=0.023$). Respondenti (46,3%) a jejich děti (70%) nejčastěji byli exponováni amoxicilinem. 44.3% respondentů používalo antibiotika k samoléčbě. Věk byl významným prediktorem jak respondent antibiotika získal ($p= 0.014$). 45.6% všech respondentů jsou ochotni užít antibiotika bez lékařského doporučení a i to je ovlivněno věkem respondentů ($p < 0.001$). Byl nalezen signifikantní vztah mezi respondenty, mající antibiotika doma a jejich pohlavím ($p < 0.001$) a věkem ($p=0.002$). Nejčastěji respondenti užívali samoléčbu antibiotiky při chřipce. Nálezy podporují hypotézu, že laická veřejnost věří, že antibiotika mohou léčit a eradikovat všechny infekce bez ohledu na jejich původce.

Závěr:

Studie ukazuje, že samoléčba antibiotiky je relativně častý problém v UAE. Intervence na různých úrovních je nutná k omezení zneužívání antibiotik. Manažerská intervence by měla

zahrnout aktualizaci antibiotické politiky ale i průvodce antimikrobiální terapií (nyní je dostupné jen druhé vydání z roku 1998) a založit národní komisi zabývající se terapií antibiotik. Edukační opatření pro lékaře a pacienty/uživatele (např. edukační kampaň týkající se použití a limitace antibiotik) mají velkou významnost. Navíc – národní systém zdravotního pojištění může hrát důležitou roli ve snižování problémů týkající se používání antibiotik

3- Srovnávací studie mezi antibiotiky na předpis a získanými v lékárně přímým prodejem

Cíle:

Hlavním cílem této studie bylo sledovat vliv některých charakteristik lékárníků (věk, pohlaví a délky praxe) na způsob dispence antibiotik (při výdeji na předpis nebo pro samoléčení) týkající se právních aspektů a racionality včetně bezpečnosti a analyzovat preferenci vydávaných antibiotik z pohledu nákladů a indikací (důvod použití antibiotik při výdeji).

Metodologie:

Průřezová studie provedená v Emirátu Abu Dhabi v období červen až září 2009. Studie proběhla ve 24 náhodně vybraných veřejných lékárnách. Data byla sbírána strukturovaným dotazníkem s uzavřenými otázkami. Pro klasifikaci antibiotik byl použit ATC/DDD systém. Náklady byly vyjádřeny ve finančních jednotkách UAE – Dirham (cca 3.7 US\$). Data byla analyzována pomocí statistického software SSPS verze 17. Vztahy byly vyjádřeny pomocí poměru šancí (OR) a 95% konfidenčního intervalu a byla provedena logistická regresní analýza.

Výsledky:

Participující farmaceuti provedly 1645 transakcí s antibiotiky, 1211 (73.6%) dispensovali na základě lékařského předpisu a 434 (26.4%) bez předpisu. Dle logistické regrese byl silným prediktorem vydání antibiotik bez receptu: věk ([OR] 1.36; P=.001), pohlaví (0.621; P=.001) a profesní zkušenost (OR 0.686; P=.001) farmaceuta a socioekonomický stav (OR 1.836;

P=.001) a pohlaví (OR, 1.346; P=.012) pacienta. Klaritromycin (91,5%), cefuroxim (91,3%) a potenciální amoxicillin (66,4%) byly nejčastěji vydávaná antibiotika na předpis. Ceftriaxone (53,3%), amoxicillin (47,8%) a potenciální amoxicillin byly nejčastěji vydány bez lékařského předpisu. Antibiotika předepsaná byla doporučena nejčastěji pro 5, 7 nebo 10denní léčebnou kůru, zatímco antibiotika vydaná bez předpisu byla vydána na 3 – 7 dní. Koamoxiclav byl nejčastěji vydáván k samoléčení na bolesti v krku. Ceftriaxone byl se stejnou frekvencí vydán bez předpisu a předepisován na pohlavně přenášené choroby.

Závěr:

Vysoká prevalence dispenzace antibiotik ve veřejných lékárnách je nezákonná a alarmující. Farmaceuti s dlouhou praxí prodávají antibiotika bez lékařského předpisu mnohem častěji než jejich mladší kolegové. Zdravotní pojišťovna by měla po konzultaci s lékaři vyvinout seznam nízkonákladových antibiotik, aby protiinfekční léčba byla dostupná pro nízko-příjmové skupiny. Analýza spotřeby antibiotik je však na začátku zásadní, aby bylo známo, jaké priority ve výběru antibiotik má terén a nemocní.

8. Conclusion:

To bring about the necessary changes in prescribers' and pharmacists' behavior, there is a need to increase the awareness of health professionals by adequate information and training during professional education and in-post training.

Pharmacists with practice experience of more than 20 years were found to have higher tendency of OTC dispensing. This can most properly be attributed to the lack of subjects that are related to the rational use of medicines in the curricula during the two last decades of the twentieth century in universities and pharmacy institutes. Thus we are emphasizing and highly recommending the inclusion of such subjects in the curricula.

Authorities should update the antibiotic policy to include penalties and punishments against those who dispense antibiotics without prescription to diminish this practice, speed up the implementation of the national medical insurance scheme which will protect and help the low income people from the irrational use of antibiotics by enabling and facilitating the consultation of a prescriber in case of suffering from any illness. In addition, it's also recommended to avail antibiotics, such as Nitrofurantion for UTIs as an alternative to the Quinolones in order to avoid and reduce the suspected resistance to them.

Support of research will be essential for tackling the problem of the improper prescribing, dispensing and the mode of spread of antimicrobial resistance.

Information measures through national educational campaigns along with simplified awareness newsletters and bulletins dedicated for the general public showing the different types of infections and their causing organisms and whether antibiotics are effective or not ,

should be conducted and distributed. This should mainly focus on highly educated segments of the society and those with low socio-economic status. This will help in changing the common concept that influenza can be treated with the use of antibiotics.

Patients' concepts should be corrected and their awareness should be raised to the fact that avoiding physicians' visits will not save their money but on the contrary it would make them more vulnerable to be dispensed medicines that are inappropriate and ineffective for their complains and this is could be due to incorrect diagnosis or incomplete treatment. Eventually they will be in need of new medications which results in higher costs.

9. List of tables

Number of Table	Title	Page Number
Table 1	UAE National population by Emirate and sex (2010 midyear estimates)	6
Table 2	Causes of Death in the United Arab Emirates by Sex in 2011	8
Table 3	Government Health Services Statistics 2007-2012 in the UAE	9
Table 4	Private Sector Health Services Statistics 2007-2012 in the United Arab	10
Table 5	Numbers and Distribution of Community Pharmacies in the UAE	15
Table 6	Examples of ADRs associated with antibiotics	28
Table 7	Some of the studies concerning antibiotics resistance conducted in UAE	39
Table 8	Demographic data of respondents	52
Table 9	Antibiotic use among adults	54
Table 10	Antibiotic use among children	55
Table 11	Antibiotics used by respondents and their children	56
Table 12	Sources of antibiotics obtained without prescription	59

Table 13	Distribution of demographics characteristics within the study Population	68
Table 14	Frequencies of used antibiotics	69
Table 15	Source of obtaining antibiotics	70
Table 16	Frequencies of common reasons for which antibiotics were Used	71
Table 17	Demographics of Respondents Keeping Antibiotics at Home	73
Table 18	Demographic Characteristics of the pharmacists	84
Table 19	Patient / Consumer characteristics	86
Table 20	Logistic Regression model for factors associated with dispensing and acquiring antibiotic without Prescription	87
Table 21	Frequencies and rank of dispensed antibiotics	90
Table 22	Distribution of J01 Antibiotic and cost	91
Table 23	Reasons for Dispensing Antibiotics	93

10. List of Figures and Maps

Number of Figure	Title	Page Number
Figure1	Reasons for antibiotics use by respondents	57
Figure 2	Reasons for antibiotics use for children	58

Number of Map	Title	Page Number
Map1	Map of UAE	5

11. List of Publications, presentations and Invited Speech

11.1 Publications

11.1.1 Publications in ISSN Journals

- 1- **Abobakr E Abasaeed. ATC/DDD Methodology: What? How and Why? *Khartoum Pharmacy Journal* 2008; 11 (1): 12-13.**
- 2- Ahmed Dahab Ahmed, Asim Ahmed Elnour, Mirghani Abd Elrahman Yousif , Farah Hamad Farah, Hasab Alrasoul Akasha Ahmed Osman, **Abobakr E Abasaeed: Improving Adherence to Prescribed Ant diabetic and Cardiovascular Medications in Primary Health Care Centers in Nyala City, South Darfur State-Sudan* *Pharmacology & Pharmacy*, 2013, 4, 701-709**

11.1.2 Publications in Impact Factor Journals

- 1- **Abobakr E Abasaeed, Jiri Vlcek, Mohammed Abuelkhair, Ales Kubena. Self-medication with antibiotics by the community of Abu Dhabi Emirate, United Arab Emirates. *The Journal of Infection in Developing Countries* 2009; 3 (07): 491-97**
<http://www.jidc.org/index.php/journal/article/view/19762966>
- 2- **Abobakr E. Abasaeed, Jiri Vlcek, Mohamed A. Abuelkhair, Retnosari Andrajati, Asim A. Elnour .A comparative study between prescribed and over-the-counter antibiotics. *Saudi Medical Journal*. 2013 Oct; 34(10):1048-54**
<http://smj.psmmc.med.sa/index.php/smj/article/view/2305>
<http://dx.doi.org/10.4236/pp.2013.49098>
- 3- Christos Lionis, Elena Petelos, Sue Shea, Georgia Bagiartaki, Ioanna Tsiligianni, Apostolos Kamekis, Vassiliki Tsiantou, Maria Papadakaki, Athina Tatsioni, Ioanna Moschandreas, Aristoula Saridaki, Antonios Bertisias, Tomas Faresjo, Ashild Faresjo, Luc Martinez, Dominic Agius, Yesim Uncu, George Samoutis, Jiri Vlcek, **Abobakr E Abasaeed and Bodossakis Merkouris: Irrational prescribing of over-the-counter (OTC) medicines in general practice: testing the feasibility of an educational intervention among physicians in five European countries. *BMC Family Practice* 2014, 15:34**
<http://www.biomedcentral.com/1471-2296/15/34>

11.2 Poster Presentations

- 1- **Abobakr E Abasaheed**, Retnosari Andrajati , Jiri Vlcek: Banking employee's attitude towards antibiotic's use in Sudan, Sultanate of Oman and UAE.
33rd European Symposium on Clinical Pharmacy European Society of Clinical Pharmacy (ESCP) Prague, **Czech Rep.** Oct **2004**

- 1- **Abobakr E Abasaheed**. ATC/DDD Methodology: What? How and Why? DUPHAT, Dubai-
UAE – .2006

- 2- **Abobakr E Abasaheed**, Jiri Vlcek, Mohammed Abuelkhair, Ales Kubena. Self-medication with antibiotics by the community of Abu Dhabi Emirate, United Arab Emirates Self-medication with antibiotics by the community of Abu Dhabi Emirate, United Arab Emirates (UAE) .7th spring conference: European Society of Clinical Pharmacy (ESCP) Edinburgh, **UK.** May **2007.**

- 3- Maha Mahmoud Al Hakim, **Abobakr E Abasaheed**, D. Jones :Evaluation of the Use of Different Insulin Regimens in the Treatment of Type 1 and Type 2 Diabetes Mellitus. American College of Clinical Pharmacy (ACCP Annual Meeting Oct 2012 Hollywood, FL, **USA**
<http://www.accp.com/docs/meetings/am12/PosterScheduleOctober24.pdf>
(Endocrinology Poster No. 85)

- 4- **Abobakr E Abasaheed** : Antibiotics: over-the-counter dispensing versus Prescriptions: ECCMID April 2012 London, **UK**
https://www.esccmid.org/esccmid_library/online_lecture_library/?search=1¤t_page=3&search_term=akar

11.3 Invited Speeches

1- Self medication with antibiotics in United Arab Emirates:

XI Clinical Pharmacy Days -Charles University -Faculty of Pharmacy -Hradec Kralove – Czech Rep. **May 2007**

<http://www.faf.cuni.cz/Konference/Archiv/2007/XI-Dny-klinicke-farmacie/Program/>

2- How to measure antibiotic consumption By Using ATC/DDD Methodology?

2nd Pharmacy Educational Forum: Medical complex, Sharjah University, Sharjah University, Sharjah, UAE. **May 2012**

http://www.cpdpharma.ae/index.php?view=details&id=12%3A2nd+Pharmacy+Educationa+l+Forum&option=com_eventlist&Itemid=84

3- Non-Adherence to Non-steroidal anti-inflammatory drugs (NSAIDs) in Geriatrics:

3rd Pharmacy Educational Forum: Medical & Health Sciences University – Faculty of Pharmacy - Ras Alkhaimah, UAE. **June 2013**

http://www.cpdpharma.ae/index.php?view=details&id=46%3A3rd_pharmacy_educational_forum&option=com_eventlist&Itemid=92

12. Appendices

12.1 Appendix 1: Use of antibiotics questionnaire

Study on the use of antibiotics

Characteristics of the participants:

1- How old are you?

2- Your gender:

Male

Female

3- please indicate your educational level :

Primary education

Secondary education

Secondary Vocational

University graduate

Post graduate

4- Do you have children below 16 years?

Yes (If yes, please continue to part B of the questionnaire after answering part A)

No

The Questionnaire

A. Participant's antibiotic use.

1- Have you taken any antibiotics in the last 12 months?

Yes (please continue to question 2)

No

2- What was/ were the name/names of antibiotic/antibiotics that you used?

3- What were the reasons for taking them?

4- For how long did you use them?

5- How did you obtain them?

- With prescription (Prescribed by a doctor or dentist or hospital)
- Without prescription
- Leftovers from previous prescription available at home
- From antibiotics intended from a relative or friend
- Other sources.

Please elaborate -----

6- In general would you use antibiotics for yourself without contacting your doctor/ dentist /hospital?

- Yes** (if yes, continue to question 7)
- No**

7- What would be the reasons or symptoms for antibiotic use without contacting the doctor?

- Runny nose
- Cough
- Bronchitis
- Sore throat
- Sinusitis
- Fever
- Flue
- Ear infections
- Toothache
- Diarrhoea
- Urinary tract infections

Other infections/diseases

Please elaborate -----

B. The use of antibiotics for your children who are under 16

8- Have you use any antibiotics for any of your children below 16 years in the last 12 months:

Yes (please continue to question 9)

No

9- What was/ were the name/names of antibiotic/antibiotics that you used?

10- What were the reasons for using them?

11- For how long did they use them?

12- How did you obtain the antibiotics for them?

With prescription (Prescribed by a doctor or dentist or hospital)

Without prescription

Leftovers from previous prescription available at home

From antibiotics intended from a relative or friend

Other sources.

Please elaborate -----

13- In general would you use antibiotics for your children below 16 without contacting your doctor/dentist/hospital?

- Yes** (if yes, continue to question 14)
- No**

14- What would be the reasons or symptoms for antibiotic use for your children without contacting the doctor/dentist?

- Runny nose
- Cough
- Bronchitis
- Sore throat
- Sinusitis
- Fever
- Flue
- Ear infections
- Toothache
- Diarrhoea
- Urinary tract infections
- Other infections/diseases

Please elaborate -----

Thank you for your cooperation, time and effort you have made.

دراسة حول استخدام المضادات الحيوية

✚ خواص المشترك :

1- كم عمرك؟

2- جنسك :

ذكر

أنثى

3- هل بإمكانك الإشارة الى مستواك التعليمي؟

أكملت التعليم الأساسي

أكملت التعليم الثانوي

أكملت التعليم الجامعي (بكالوريوس)

تعليم عالي مهني أو جامعي (ماجستير، دكتوراه أو ما شابه)

4- هل لديك أطفال أصغر من عمر 16 سنة؟

نعم (إذا أجبت بنعم، الرجاء اكمال الجزء ب من الاستبيان بعد الاجابة عن الجزء أ)

لا

✚ الاستبيان

أ. استخدام المضادات الحيوية من قبلك:

1- هل استخدمت شخصياً أي نوع من المضادات الحيوية خلال فترة الأثني عشر شهراً الماضية؟

نعم (انتقل الى السؤال رقم 2)

لا

2- ما هو اسم \ أسماء المضاد الحيوي \ المضادات الحيوية الذي \ التي قمت باستخدامه ؟

3- ما كانت الأسباب التي دفعتك لاستخدام الدواء؟

4- كم مدة استخدامك للدواء؟

5- كيف حصلت على الدواء ؟

- بوصفة طبية (من الطبيب \ طبيب الأسنان \ او المستشفى)
- بدون وصفة طبية
- ما تبقى من وصفة طبية سابقة
- كان مخصصا لأحد الأقارب أو الأصدقاء
- جهة أخرى

الرجاء التوضيح:-----

6- بشكل عام، هل يمكن أن تستخدم مضاد حيوي بدون استشارة الطبيب\ اطبيب الاسنان أو المستشفى؟

نعم (انتقل إلى السؤال رقم 7)

لا

7- ما هي الأسباب التي قد تدفعك لاستخدام المضاد الحيوي بدون استشارة الطبيب؟

- زكام
- سعال
- التهاب رئوي
- آلام الحلق
- التهاب الجيوب الأنفية
- الحمى
- انفلونزا
- التهاب الأذن
- آلام الأسنان
- إسهال
- التهاب المجاري البولية
- التهابات أخرى

الرجاء التوضيح:-----

ب. استخدام المضادات الحيوية لأطفالك أقل من عمر 16 سنة:

8- هل استخدمت أي نوع من المضادات الحيوية لأي من أطفالك خلال فترة الأثني عشر شهراً الماضية؟

نعم (انتقل الى السؤال رقم 9)

لا

9- ما هو اسم \ أسماء المضاد الحيوي \ المضادات الحيوية الذي\ التي قمت باستخدامه لهم؟

10- ما كانت الأسباب التي دفعتك لاستخدام الدواء؟

11- كم مدة استخدامهم للدواء؟

12- كيف حصلت على الدواء ؟

- وصفة من الطبيب \ طبيب الأسنان \ او المستشفى
- بدون وصفة طبية
- ما تبقى من وصفة طبية سابقة
- كان مخصصا لأحد الأقارب أو الأصدقاء
- جهة أخرى

الرجاء التوضيح:-----

13- بشكل عام، هل يمكن أن تستخدم لأي من أطفالك مضاد حيوي بدون استشارة الطبيب\ الممرضة أو المستشفى؟

نعم (انتقل إلى السؤال رقم 14)

لا

14- ما هي الأسباب التي قد تدفعك لاستخدام المضاد الحيوي بدون استشارة الطبيب أو طبيب الأسنان؟

- زكام
- سعال
- التهاب رئوي
- آلام الحلق
- التهاب الجيوب الأنفية
- الحمى
- انفلونزا
- التهاب الأذن
- آلام الأسنان
- إسهال
- التهاب المجاري البولية
- التهابات أخرى

شكراً لكم على تعاونكم و الوقت و الجهد الذي بذلتموه

12.2 Appendix 2: List of the Commonly Used Antibiotics

قائمة بأسماء المضادات الحيوية الأكثر استعمالاً

- ◆ هذه القائمة تساعدكم كثيراً في الإجابة علي الأسئلة المطروحة.
◆ في حالة استخدامكم لمضاد حيوي غير وارد ذكره في هذه القائمة ، أو في حال عدم تأكدكم بأن الذي استخدمتموه ليس مضاداً حيويًا ، الرجاء كتابة اسم الدواء في الخانة المناسبة.
◆ تذكر أننا نعني المضادات الحيوية بكل أشكالها الصيدلانية (الحقن – الحبوب – الكبسولات – الشرايبات الخ

1- Benzyl Penicillin

3- Amoxycillin (Penamox , Amoxil , Amoxydar)

5- Ampiclox (Amoclan , Klavox , Amoxiclav)
, Julmentin ,

7- Benthazine Penicillin (Penadur , Retarpen)

9- Cefixime (Suprax , Magnacef)

11- Cephtazidime (Fortum)

13-Cefuroxime (Zinacef , Zinnat , , Maxil , Cefuzime)

15- Doxycycline (Zadorin , Doxydar)

17- Erythromycin Erythrodar. Erythrocin)

19- Azithromycin (Zithromax)

21- Co-trimoxazole (Septrin , Bactrim , Balkatrim)

23- Spectinomycin (togamycin)

24- Ciprofloxacin (Ciprobay , Ciprodar , Sarf , Ciplox)

25- Norfloxacin (Trizolin , Noracin , Gyrablock , Noroxin)

2- Procaine Penicillin

4- Ampicillin (Penberitin)

6- Amoxicillin/clavulanic acid

8- Cephacor (Ceclor)

10- Cephalexin (Kefflex)

12- Ceftriaxone(Rocephin)

14- Tetracycline

16- Gentamycin(Gentadar)

18- Amikacin

20-Clarithromycin (Kalcid)

22- Ofloxacin (Tarivid)

12.3 Appendix 3: Abu Dhabi Health Authority Approval

29-3-2006

Dr. Mohammed Abuelkhair
Drug Consultant Advisor
General Authority for Health Services – Emirate of Abu Dhabi

Subject: Antibiotic's Questionnaire

Ref. to the above mentioned subject , I'm looking for the approval of it's display , since this questionnaire will be running among the visitors of the Abu Dhabi Book Fair , which will take place in Cultural Foundation -Abu Dhabi (29 Mar. -7 Apr.) .

Looking for your kind approval

Best regards

Dr. Abobakr Abasaheed Elhaj



Approved By: **Dr. Mohammed Abuelkhair**



12.4 Appendix 4 : Portrait of the Commonly Used Antibiotics



12.5 Appendix 5: Abu Dhabi Health Authority Approval

18-10-2008

Dr. Mohammed Abuelkhair

Drug Consultant Advisor

AbuDhabi Health Authority

Subject: Antibiotics Dispensary at community pharmacies

Ref. to above mentioned subject, I'm looking for the approval of conducting this study during the period from 10-20 Nov 2008 in randomly 20 selected pharmacies.

Looking for your kind approval

Best Regards

Dr. Abobakr Abasaeed Elhaj



Approved By: Dr. Mohammed Abuelkhair

لا مانع من زيارة الصيدليات الخاصة في أبوظبي
من أجل إجراء الأبحاث مع الصيدلانية



12.6 Appendix 6

Pharmacist information sheet

Dear Pharmacist:

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

This study will examine the antibiotic prescribing pattern in the pharmacy. The results of the research may be published. You will not be identified in any report/publication. You will be given a copy of the information sheet and a signed consent to keep.

We wish to thank you for taking part in the study.

Thanking you in taking the time and reading this information sheet.

For further information please contact:

Dr. Abobakr Abasaeed

Abu Dhabi -UAE. Tel: (+971) 50 73 76 987

12.7 Appendix 7

Pharmacist consent from

I, the undersigned, voluntarily agree to participate in this study.

I have read the patient information sheet (or have had it read to me) and I understand the purpose of the study and what I am expected to do.

I understand that if, at any stage, I do not wish to participate any further in the study I can withdraw. I do not have to explain why and I know that it will not affect my future care or cause any displeasure.

I have been assured that all the information that is collected during the study will be kept confidential.

Pharmacist's name
(*Optionally*)

Signed

Date

Pharmacy Code

12.8 Appendix 8: Questionnaire of Study III

A comparative study between prescribed and over –the-counter antibiotics

Ser Number:

2- Pharmacy Number.....

Pharmacist demography

3- Age:

4- Sex:

1- Male

2- female

5- Experience:

Years

Patient Demography

6- Age:

7- Sex:

1- Male

2- Female

8- Socio- Economic Status:

1- High=>5000

2- Medium= >2000

3- Low low<2000

Dispensed Antibiotics

9- Trade Name:-----

10- Generic Name:-----

11- Quantity:

Tablets

12- Duration:

Days

13- Cost:-----

Way of Dispensing

14- Prescription:

1- Yes

2-No

Reasons for Dispensing

15- Tick from the list the reasons (Max 3 reasons)

1- Sore Throat

9- Diarrhea

2- Fever

10- H.Pylori

3- Sinusitis

11- UTI

4- Cough

12- STD

- 5- Tonsillitis
- 6- Bronchitis
- 7- Influenza
- 8- Otitis Media

- 13- Acne
- 14- Wounds Injuries
- 15-Toothache

16- Others-----

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