Original Article

Evaluating Antibiotics Administration's Pattern and Its Financial Burden in a Teaching Hospital in Iran

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Abstract

Indiscriminate use of antibiotics frequently leads to healthcare complications, including an increase in the number of resistant microorganisms and patient hospitalization period, which subsequently results in a financial disadvantage for the patients and the country's healthcare system. Therefore, researches on causes of such malpractices could shed light on ways to prevent further impacts on health care system. The purpose of this study is to investigate antibiotics administration's pattern and its financial burden in a teaching hospital in Iran in 2018. This descriptive cross-sectional study is based on data obtained from the hospital medicine statistics unit. The share of antibiotics in the total cost of medicine expenditure has been calculated and the cost burden of top 10 antibiotics and their administration in different hospital departments were also assessed. According to the data obtained, about 12.2% of the total cost of medication expenditure in the hospital in 2018 was attributed to the administered antibiotics. The financial burden due to the use of all medicines and antibiotics in 2018 per patient admitted in the hospital were 4,327,912 Rials (1,030 USD) and 529,400 Rials (126 USD), respectively. The total use of these antibiotics was 56.77 DDD/100Bed-Days. Financial burden of the injectable forms of antibiotics is higher than other pharmaceutical forms and the intensive care unit showed the most use of these antibiotics. The 10 most high-cost administered antibiotics included Meropenem, Ciprofloxacin, Clindamycin, Vancomycin, Teicoplanin, Levofloxacin, Metronidazole, Azithromycin and Ceftriaxone, respectively. Compared to the other published data regarding administration of antibiotics in other hospitals, this study showed that there is a need for more surveillance on rational administration of the antibiotics in this hospital.

Keywords: Antibiotics, Consumption, Hospital, Cost management.

1. Introduction

In many countries, antibiotics make up about 30 to 50% of prescription medicines. Although antibiotics are essential for management of most bacterial infections, there are studies shown that 30 to 60% of antibiotics administration are inappropriate [1, 2]. Improper use of antibiotics causes health

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problems such as increasing the number of hospitalization days, financial costs for both health care system and patients, and increasing the prevalence of microbial resistance. A study of antibiotic-resistant infections in hospitals found that these infections have increased hospital stay by about 4.6 to 7.12 days, and deaths from resistant infectious diseases increased by 5.6. % [3].

Estimated costs attributed to the medical cost per patient with an antibiotic-resistant infection range from $18,588 to $29,069. The total economic burden placed on the US economy through antibiotic-resistant infections has been estimated to be as high as $20 billion in health care costs and $35 billion a year in lost productivity [4, 5]. In the case of antibiotic-resistance, the number of recipients is also important [6]. Physicians, emergency departments, and other outpatient clinics in the United States prescribed approximately 270 million antibiotics in 2015, or 838 antibiotics per 1,000 patients [7].

Thus, antibiotics, as one of the most valuable class of medicines, are in danger of reducing their effectiveness and efficiency due to increased microbial resistance. Therefore, efforts to rationalize antibiotic use has always been one of the most important aspects of drug policy [8, 9]. Examining the pattern of antibiotic use in each department will helps for better infection control strategies in the hospital and also reduces antibiotic resistance [10]. In order to standardize drug utilization studies including antibiotics, World Health Organization for statistical studies of drugs has proposed a valid indicator, ATC / DDD classification [11]. Defined Daily Dose (DDD) is designed to compare drug consumption information across time and place. In addition, drug utilization is expressed with rate. Common units for antibiotic consumption rate can be defined by DDD per 100 bed-days in hospitals [12, 13].

According to this method, in a study conducted in Qom hospitals (Iran) in 2019, Ceftriaxone with 33.6, and Amikacin with 21.2 DBDs were mentioned as the most common antibiotics used [14]. Another study conducted in 2011-2016 at a hospital affiliated with the Military Medical University in Belgrade, Serbia, showed that Hospital-acquired infection was more common in patients with surgical ICUs and that the most antibiotic used were Cephalosporins with 14-18 and Aminoglycosides with 5.5. 4.1 and Carbapenems are 5-3.6 DBDs, respectively [15]. Also, the results of a separate study using ATC / DDD index showed that the rate of inappropriate use of antibiotics, costs and also the rate of nosocomial infections with resistant species in Turkish hospitals are high [16].

Therefore, due to the need to study the economic burden and consumption issues of antibiotics, this study has examined the

financial burden and the prescription pattern of antibiotics in a teaching hospital in Tehran, Iran in 2018.

2. Materials and Methods

This is a descriptive, retrospective and cross-sectional study that examines the financial burden and consumption of high-cost antibiotics in 2018 in a military affiliated teaching hospital in Tehran, Iran. In this study, after identifying 10 high-cost antibiotics in the hospital, financial burden and the amount of consumption of each of the antibiotics in the departments, has been calculated. The cost of antibiotics is calculated using local currency, Rials and USD. It should be mentioned that in order to reduce price of medicines in Iran, government of Iran allocates "subsidized hard currency" for medicines in Iran. Therefore, one USD in Iran pharmaceutical sector worth 42,000 Rials while its real cost in market is about 250,000 Rials. For purpose of this study conversion of local currency to USD is made on based 1USD=42,000 Rials.

Antibiotic use was expressed as defined daily doses per 100 bed-days (DBDs) according to the ATC/DDD classification. In order to determine the DDD conversion factor, the usual dose per gram of each antibiotic is divided to its ATC/DDD amount. Multiplication of the quantity dispensed by a conversion factor equals a total of DDDs for each drug.

Total of DDDs for each drug= (Usual dose)/ (ATC/DDD) × Quantity dispensed

For Calculation of DDD per 100 bed-days (DDD/100), total amount of each drug dispensed based on DDD is divided into bed day and multiply by 100.

DDD per 100 bed−days = (Total of DDDs for each drug)/ (Bed days) ×100

It should be mentioned that, bed day is calculated by multiplying the total number of patients in each period by number of days in that period.

3. Results and Discussion

According to the information received from the Drug Management Unit of the hospital, in 2018, the total cost of consumed medicines in the hospital was 431,224,548,376 Rials (10,267,251$). The total cost of consumed antibiotics this year was 52,748,511,460 Rials (1,255,916$), which is 12.2% of the total cost of consumed drugs. In 2018, the number of people who referred to all departments of the hospital, including departments with occupational day bed index and day care departments, was 99,638.

Therefore, the cost due to the administration of all medicines is 4,327,912 Rials (103$) per patient and the financial burden due to the use of antibiotics is 529,400 Rials (12.60$) per patient.

Top 10 highest-cost antibiotics in 2018 are Meropenem, Ciprofloxacin, Cefazolin, Clindamycin, Vancomycin, Teicoplanin, Levofloxacin, Metronidazole, Azithromycin and Ceftriaxone, respectively.

The share of the cost of consumption of each of these 10 antibiotics from the total cost of consumption of antibiotics is shown in Fig.1. Meropenem with 16,453,540,000 Rials (391,750$) had the highest and Ceftriaxone

with 1,416,607,300 Rials (33,728$) had the lowest cost among these 10 high-cost antibiotics. In Table 1, the cost of each of these antibiotics and their share in the total cost of medicines are presented separately. Figure 2 also compares the cost of each of these antibiotics.

The total dose of these high-cost antibiotics in the whole hospital is 56.78 DBDs. Cefazolin with 12.18 DBDs had the highest and Teicoplanin with 1.33 DBDs had the lowest consumption among these 10 antibiotics. Table 2 shows the consumption of each of these antibiotics separately.

Among the departments with of high-consumption antibiotics, the Gynecology department has the 1st rank. The use of Cefazolin in this department is 46.61 DBDs. However, the highest amount of financial burden among these departments belongs to Internal Intensive Care Unit, and the financial burden of Meropenem is 4,237,446 Rials (101$) per patient admitted to this department.

Table 3 shows data for each of the 10 most high-cost antibiotics, the departments which used the most of these antibiotics, along with financial burden for each hospitalized patient. According to the results of this study 12.2% of total costs of medicines used in the hospital are related to antibiotics. Total cost of the total consumed medicines and antibiotics in the hospital was 4,327,912 Rials (103$) and 529,400 Rials (12.60$) per patient, respectively. In reported studies, which examined the status of antibiotics administration in Taleghani and Shohada Tajrish Hospitals, the cost of antibiotics was

19.4% and 30%, respectively (9,17). Therefore, this hospital has a lower financial burden due to of antibiotics consumption. Among antibiotics, Meropenem had the highest cost with 31.19%, while Ciprofloxacin, which ranks second, accounts for 8.23% of the total cost of antibiotics. Cefazolin, Clindamycin, Vancomycin, Teicoplanin, Levofloxacin, Metronidazole, Azithromycin and Ceftriaxone were in the next rank of the costs, respectively. The total cost of consuming these 10 antibiotics is equal to 38,933,768,086 Rials (926,994$), which accounts for 73.85% of the total cost of antibiotics and 9.03% of the total cost of the administered medicines.

This is obvious that that most of inpatients who need to receive antibiotics have either undergone surgery or developed severe infections, in which case, injectable dosage forms of antibiotics are usually preferred. In these 10 top antibiotics injectable dosage forms account for 88.92% of the cost and 10.58% for oral dosage forms. In a reported study, more than 97% of the cost of prescription antibiotics was related to the injectable forms [9]. It was also previously reported that in Qom hospitals, 93.5% of prescription antibiotics were injectable [14]. Another study reported that more than 85% of antibiotics were injected in all 5 hospitals studied in Tabriz were injectable dosage forms [18]. In the Intensive Care Unit, the financial burden due to the use of Meropenem was 4,227,446 Rials (101$) per patient admitted, but in the Heart Transplant Surgery department, the financial burden due to the use of Ciprofloxacin oral, is 538 Rials (0.01$) per patient. Also, in the Post CCU

department, oral Azithromycin was the most prescribed antibiotic with 5,856 Rials (0.13$) per patient.

The total consumption of 10 high-cost antibiotics was 56.78 DBDs, of which 83.57% were injectable dosage forms, 16.41% oral dosage forms, and 0.02% vaginal dosage forms.

3.1. Cefazolin

Among the 10 high-cost antibiotics, Cefazolin with 12.18 DBDs was the most used in the hospital. In a study at a hospital in Sari (Iran), cefazolin was the most commonly used antibiotic, with 20.5 DBDs in the first half of 2000 and 40 DBDs in the first half of 2005 [19]. In another study which investigated on the use of intravenous antibiotics in a hospital in Saudi Arabia, the use of Cefazolin increased gradually from 2006 to 6.2 DBDs in 2008 [20]. In our study Cefazolin has been prescribed in Gynecology, Orthopedics, and Intensive Care Units more than other departments. Cefazolin is prescribed as surgical prophylaxis in these departments.

3.2. Meropenem

The next most widely used antibiotic after Cefazolin is Meropenem with 9.48 DBDs. In a 2018 study in Serbia, Meropenem was the second most common antibiotic with an average of 2.1 DBDs [15]. Meropenem was also reported as the fourth most common antibiotic with a dose of 6.1 DBDs [14]. One of the reasons for the high consumption of Meropenem is its wide spectrum range of activity against microorganisms.

3.3. Ceftriaxone

Ceftriaxone is the third most widely used antibiotic among 10 high-cost antibiotics with 7.37 DBDs. Open heart intensive care unit used the most of this antibiotic. It is reported that Ceftriaxone consumption decreased significantly between 2012 and 2015. The dose of this drug in Qatar in 2015 was 6.7 DBDs [21]. It seems that this reduction in consumption is due to the use of a monitoring program to promote rational prescription of antibiotics. However, a high consumption of Ceftriaxone (33.62 DBDs) reported in another study [14].

3.4. Metronidazole

Metronidazole is one of the antibiotics used to prevent infection and treat surgical infections. The most common use of this drug in our study was in General Intensive Care Units, Male Surgery and Gynecological surgery. The total amount of usage in the hospital is 6.79 DBDs and in terms of consumption, it is in the fourth category of high-cost antibiotics. The dose of this antibiotic was reported between 2013 to 2017 in a hospital in Spain 3.25 DBDs, which was the most used in Surgical Departments [22]. Consumption of Metronidazole in another study reported to be 4.01 DBDs in the first half of 2000, and 8.96 DBDs in the first half of 2005, with the highest use of this antibiotic in Intensive Care Units [19]

3.5. Clindamycin

The rate of use of Clindamycin in the hospital is 5.8 DBDs which is much higher than

other countries. Clindamycin use in a hospital complex in the UK in 2004 and 2005 was 0.4 and in 2003 it was 0.6 DBDs [23]. Drug use in Taiwan declined from 2011 to 2013, from 2.5 DBDs in 2011 to 0.4 DBDs in 2013 (24). However, in a study in Sari hospital, the dose of this drug in 2005 was calculated as 5.2 DBDs [19].

3.6. Azithromycin

Azithromycin is a common drug used to treat respiratory infections. The rate of consumption of thus antibiotic in this study is 4.32 DBDs, which is lower than Qatar Hospital and Valiasr Hospital in Zanjan. Drug use in a Qatar hospital declined from 2012 to 2015, reaching 4.4 DBDs in 2015 [21]. The rate of use of this drug has been reported in Valiasr Hospital of Zanjan 11 DBDs [25].

3.7. Levofloxacin

In this study, Levofloxacin was used in the amount of 4 DBDs. The most common use of this drug has been in the Intensive Care Units, Post CCU and Gynecology. The drug consumption was lower than of in a 2013 study in India of 12.54 DBDs and a study in Italy of 7.40 DBDs [26, 27].

3.8. Vancomycin

The rate of consumption of Vancomycin is 3.8 DBDs. Most prescriptions are in Surgical Intensive Care Units. In India it was reported to be 0.1 DBDs in 2013 [28] and in 2008 in Saudi Arabia 3 DBDs [20]. In 2019 in Qom, the rate of consumption of this drug was 11.3 DBDs [14], which is about 3 times more than our study.

3.9. Ciprofloxacin

Ciprofloxacin was introduced as one of the five most widely used antibiotics in five hospitals in Tabriz. The use of this antibiotic in Imam Reza Hospital in Tabriz was 18.2 and in Shahriar and Shohada Hospital in Tabriz were reported 10 and 2 DBDs, respectively [18]. In a hospital in Mongolia in 2017, the use of this antibiotic was 15.2 DBDs [29]. The rate of consumption of this drug in our study was 1.7 DBDs, which is lower than reported studies. In Imam Khomeini Hospital in Sari, the highest use of Ciprofloxacin has been reported in Intensive Care Units, Internal and Orthopedic departments, respectively [19]. In the present study, the highest use of Ciprofloxacin was in Heart Transplant Surgery and Gynecological Surgery departments. Surgeons seem to prescribe this antibiotic as the first line treatment for wound infections.

3.10. Teicoplanin

Teicoplanin is a glycopeptide with a spectrum similar to vancomycin. In a 2013 in India, the use of Teicoplanin was reported to be 0.02 DBDs [28]. Also in a study in Italy, glycopeptides were used most in Intensive Care Units [27]. The rate of consumption of this antibiotic in this study was 1.3 DBDs and its highest use in the Intensive Care Unit was 8.5 DBDs.

4. Conclusion

According to this study, 12.20% of the total cost of consuming drugs in an army affiliated Hospital in Iran in 2018 is related to antibiotics. The 10 most high-cost antibiotics are Meropenem, Ciprofloxacin, Clindamycin, Vancomycin, Teicoplanin, Levofloxacin, Metronidazole, Azithromycin, and Ceftriaxone, respectively. The total cost of these 10 antibiotics is 73.81% of the total cost of antibiotics and 9.03% of the total cost of drugs. Injectable dosage forms of these 10 antibotics account for 88.92% of the cost of high-cost. The total consumption of 10 high-cost antibiotics is estimated at 56.78 DBDs. Among these antibiotics, Cefazolin was the most widely prescribed antibotics. The Intensive Care Unit used these 10 antibiotics more than other hospital departments, and 6 of them including Meropenem, Vancomycin, Teicoplanin, Levofloxacin, Metronidazole, and Ceftriaxone were identified as the most widely used.

Finally, according to the comparisons made, the consumption of 10 high-cost antibiotics in this hospital was higher than similar reported studies. Results of this study confirm urgent need for implementation of guideline for promoting rational prescription of antibiotics and curbing high financial burden of antibiotics consumptions in this hospital.

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Tables:

Table 1. The cost of consuming 10 high-cost antibiotics in an army affiliated hospital in Iran in 2018.

Antibiotic	Route of Administration	Cost; Rials (USD)	Total Costs; Rials (USD)	Share in all antibiotics	Share in all medicines
Meropenem	Parenteral	16،453،540،000 (391,750$)	16،453،540،000 (391,750$)	31.19%	**3.81%**
Ciprofloxacin	Oral	542،263،600 (12,911$)	4،343،681،700 (103,420$)	8.23%	**1%**
	Parenteral	3,773,782,400 (89,851$)			
	Ophthalmic	27،635،700 (657$)			
Cefazolin	Parenteral	2،898،077،300 (69,001$)	2،898،077،300 (69,001$)	5.49%	**0.67%**
Clindamycin	Oral	304,357,900 (7,246$)	2،759،030،976 (65,691$)	5.23%	**0.64%**
	Parenteral	2،306،384،000 (54,913$)			
	Vaginal	33,807,800 (804$)			
	Topical	114,481,276 (2,725$)			
Vancomycin	Parenteral	2،570،123،500 (61,193$)	2،570،123،500 (61,193$)	4/87%	**0.60%**
Teicoplanin	Parenteral	2،351،656،500 (55,991$)	2،351،656،500 (55,991$)	4.46%	**0.54%**
Levofloxacin	Oral	1،149،806،600 (27,376$)	2،269،433،200 (54,034$)	4/30%	**0.53%**
	Parenteral	1،119،626،600 (26,657.77$)			
Metronidazole	Oral	255،349،360 (6,079$)	2،024،641،960 (48,205$)	3.79%	**0.46%**
	Parenteral	1،751،839،000 (41,710$)			
	Vaginal	17،453،600 (415$)			
Azithromycin	Oral	1،869،930،650 (44,522$)	1،870،924،650 (44,545$)	3.55%	**0.43%**
	Parenteral	994،000 (23$)			
Ceftriaxone	Parenteral	1،416،607،300 (33,728.74$)	1،416،607،300 (33,728.74$)	2.68%	**0.33%**
Total	Oral	4،121،708،110 (98,135$)	38,957,717,086 (927,564$)	73.85%	**9.03%**
	Parenteral	34،642،630،600 (824,824$)			
	Vaginal	51،261،400 (1,220$)			
	Other Routes (Topical and Ophthalmic)	142،116،976 (3,383$)			

Table 2. Consumption of 10 high-cost antibiotics by dosage form.

| Name	Route of Administration	ATC Code/DDD	DBDs/dosage form	Total DBDs
Meropenem	Parenteral	J01DH02 / 3	9.48	9.48
Ciprofloxacin	Oral	J01MA02 / 1	1.27	1.75
	Parenteral	J01MA02 / 0.8	0.48	
Cefazolin	Parenteral	J01DB04 / 3	12.18	12.18
Clindamycin	Oral	J01FF01 / 1.2	0.35	5.79
	Parenteral	J01FF01 / 1.8	5.43	
	Vaginal	G01AA10 / 0.1	0.005	
Vancomycin	Parenteral	J01XA01 / 2	3.78	3.78
Teicoplanin	Parenteral	J01XA02 / 0.4	1.33	1.33
Levofloxacin	Oral	J01MA12 / 0.5	2.98	3.98
	Parenteral	J01MA12 / 0.5	1	
Metronidazole	Oral	P01AB01 / 2	0.39	6.79
	Parenteral	J01XD01 / 1.5	6.4	
	Vaginal	G01AF01 / 0.5	0.005	
Azithromycin	Oral	J01FA10 / 0.3	4.33	4.33
	Parenteral	J01FA10 / 0.5	0.001	
Ceftriaxone	Parenteral	J01DD04 / 2	7.37	7.37
Total	**Oral**		**9.32**	**56.78**
	Parenteral		**47.45**	
	Vaginal		**0.01**	

Table 3. Consumption and financial burden of high-cost antibiotics in the departments with the highest consumption.

Name	High consumption Department	Route of Administration	DBDs	Rate of consumption in all Departments	Financial burden; Rials (USD)
Meropenem	Internal ICU	Parenteral	41.69	9.32%	4٬237٬446 (101$)
Ciprofloxacin	Heart Transplant Surgery	Oral	5	5.59%	538 (0.01$)
Cefazolin	Gynecology	Parenteral	46.61	9.89%	65٬738 (1.56$)
Clindamycin	Internal	Oral	0.14	20.12%	365٬766 (8.70$)
		Parenteral	26.84		
		Total	26.98		
Vancomycin	Surgical ICU	Parenteral	26.88	7.99%	198٬915 (4.73$)
Teicoplanin	Internal ICU	Parenteral	8.48	13.44%	453٬570 (10.79$)
Levofloxacin	Internal ICU	Oral	2.12	11.69%	353٬367 (8.41$)
		Parenteral	19.78		
		Total	21.90		
Metronidazole	General ICU	Oral	0.19		113٬160 (2.69$)
		Parenteral	44.85		
		Total	45.40	12.36%	

Azithromycin	Post CCU	Oral	17.70	11.82%	5٬856 (0.13$)
Ceftriaxone	**Open Heart ICU**	**Parenteral**	**33.98**	**6.49%**	**44٬362 (1.05$)**

ICU: Intensive Care Unit; CCU: Cardiac Care Unit

Figures:
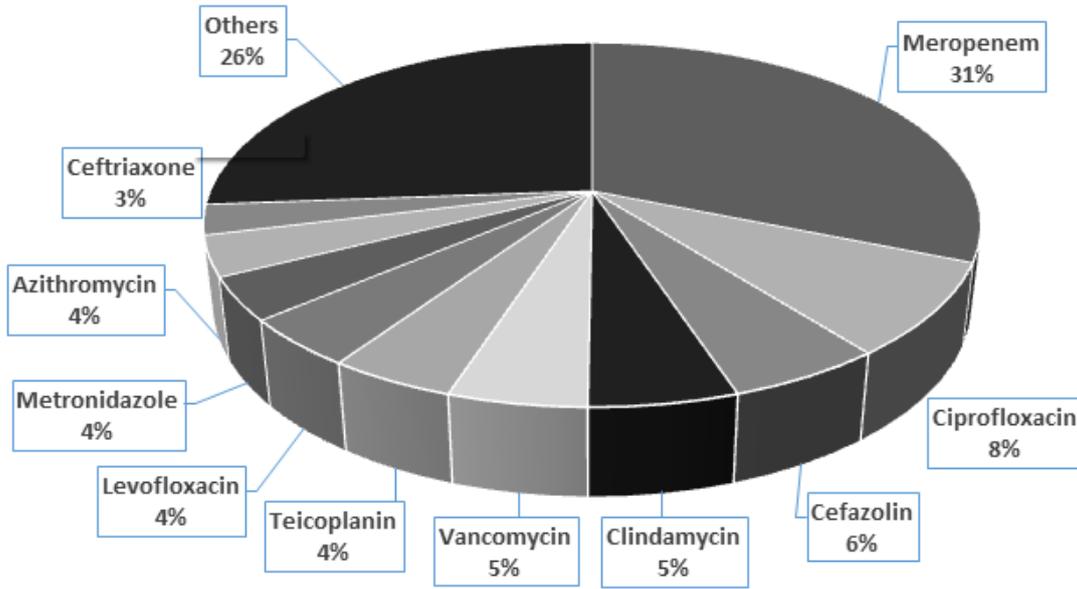
Figure 1. The share of 10 costly antibiotics in the total cost of antibiotics.
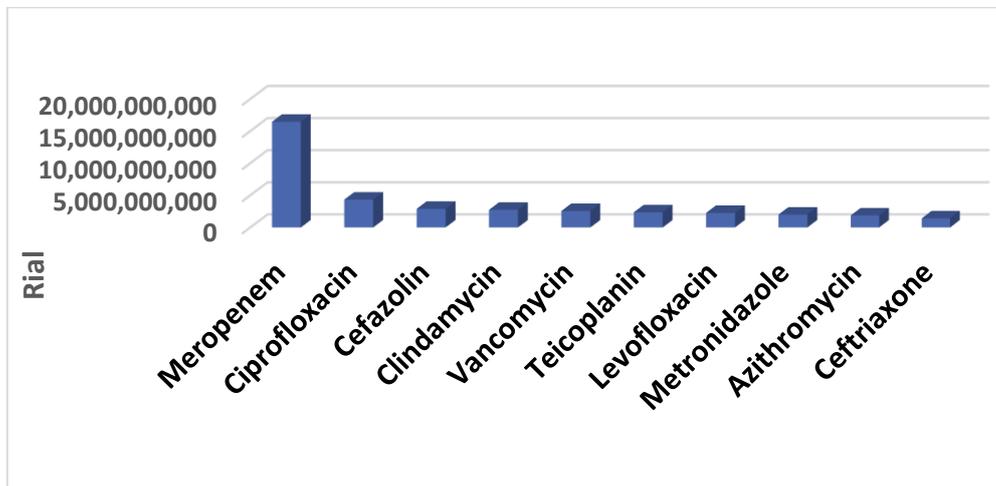
Figure 2. Comparison of the cost of consuming 10 high-cost antibiotics in in a Teaching Hospital in Iran in 2018.

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