

The Study of Availability, Affordability and Price Variation of Essential Antibiotics in Bangladesh

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<http://dx.doi.org/10.13005/bpj/1812>

(Received: 08 September 2019; accepted: 21 October 2019)

The increased prices and low availability of medicines are main obstacles to health care system in developing countries like Bangladesh. The main goal of this work is to gather and assessing the data on availability, affordability and price variations of essential antibiotics in Bangladesh. The data will help to improve the availability and affordability of essential antibiotics for the mass peoples. The present work was done using standard methodology described in guideline, "Price measurement, availability and affordability and price components of medicines. A total of eighteen essential antibiotics were surveyed and their prices and availability were determined. Prices from 2003 to 2019 were collected from different sources to make a comparative study of the price variations over the years. The overall prices of essential antibiotics are not much higher than international reference prices. The rate of increase of price from previous years is not so alarming. The numbers of manufacturing companies were collected from the Bangladesh National Formulary (BNF) of different Volumes to compare the increasing number of manufacturers. Essential antibiotics affordability was determined by comparing the total cost of treatment of a particular disease to the monthly salary of the lowest paid unskilled laborer. There are several essential antibiotics for which the numbers of manufacturing companies are increasing in very high rate. This type of survey may be expanded to the national level for the data of different regions of Bangladesh.

Keywords: Affordability, Availability, Essential Antibiotics,
Median Price Ratio, Median Price and Price variations.

The insufficiency of access to essential antibiotics remains a great public health problem all over the world. World Health Organization (WHO) defines the essential medicines as "those medicines which meet the global health needs of the majority

of the population of a particular territory". The WHO updates its Model Essential Medicines List every 2 years in a transparent way. Although access to essential medicines has improved since the introduction of the essential medicines concept in

1977, one-third of the world's population is still not treated with the required medicines that are needed for their treatment. In low- and middle-income countries (LMICs), as many as ninety percent of the population pay out-of-pocket for their drugs. The USA has also made a shift to high-deductible insurance strategy during within the last decades¹.

In 2001, a resolution (WHA 54.11) endorsed by the Member States of the World Health Assembly called for a standardized procedure to monitor medicines prices to help boost the access. In response, the World Health Organization/Health Action International (WHO/HAI) Project on Medicine Prices and Availability was established. The primary purpose of this project was to develop a standardized method to calculate medicines' prices, availability, affordability and price components in a reproducible method so as to allow international comparisons against the time. In 2003, after testing in 9 countries, the standard WHO/HAI methodology was released, with a second edition published in 2008².

Poor medicine availability, increased prices and low affordability are major obstacles to medicine access for common people in developing countries of the world. In many developed countries, for example, the USA, there are growing concerns about decreased medicine access for reasons including high medicine prices and co-payments/deductibles, uninsured populations, inadequate transparency in medicine price components, and health agencies' low capability to bargain procurement prices¹.

For the evaluation of the studied medicines' consumer prices, WHO/HAI methodology uses international reference prices (IRPs) as an external standard. To evaluate prices, a median price ratio (MPR) is measured by comparing the median consumer price of a supplied medicine with the particular IRP. International reference prices used in this work were taken from the 2015 Management Sciences for Health (MSH) International Drug Price Indicator Guide.

The MSH reference prices were published in 1986 for the first time. The MSH reference prices are procurement prices obtained from both sellers and purchasers and collected from government agencies, pharmaceutical suppliers and international development organizations. The MSH prices are widely accepted as proper reference

standards³. These MSH procurement prices report the real prices obtained by non-profit suppliers and government tenders, the robust nature of this data ensures international comparability⁴.

Government of any country should procure medicines from the reliable sources as compared to the IRPs patient prices from the private sector to reduce the excessive cost of the medicines occurring from the additional costs in markups, tariffs, taxes and other costs. Because of these additional costs, the WHO has set a target of 4 times the IRP for patient prices in the private sectors. Medicine availability and prices are recognized as an important components of access to medicines by WHO, For this reason the WHO five years strategic plan 2008-2013 defines the global and national targets for generic essential medicines, targeting 80% availability in all sectors and median consumer prices to be no more than four times the IRP. In studied works, the Median price ratios of studied medicines in Bangladesh varied from 0.36-2.56 and 0.33-2.36 in year 2015 and 2019, respectively.

Medicines included in this survey are used all over the world. The medicines are used to treat common conditions and appear on most treatment guidelines. Many of the surveyed medicines were studied in the 2009 study of medicine availability and prices in 36 developing and middle-income countries³.

In our work, we examined the availability of essential antibiotics across Model pharmacies and general retail stores. Prices were obtained from BDNF-2, BDNF-3, BDNF-4 and DGDA website of year 2003, 2006, 2015 and 2019, respectively, and essential antibiotics prices of 2015 according to BDNF 4 and 2019 according to DGDA website were then compared with the MSH IRPs. The current survey was performed using standard methodology stated in guideline Price measurement, availability and affordability and price components of medicines².

The WHO/HAI Project on Medicine Prices and Availability was founded in 2001 – (i) to develop a effective methodology for accumulating and analyzing medicine price, availability, affordability and medicine price component data in different health-care sectors and regions in a country; (ii) to publish survey data on open access website to enhance price transparency; and (iii)

to recommend for proper national policies and monitor their consequences.

The specific objectives of our study were – (i) to measure prices of Essential antibiotics for treating prevalent conditions in Bangladesh, (ii) to assess the affordability of standard treatment regimens utilizing these medicines, (iii) to compare the prices of drugs found in the country with international reference prices and (iv) to compare the prices of essential antibiotics of different years with statistical significance testing.

National drug policy 2016

Bangladesh Government has approved 3rd national drug policy of the country in its Cabinet Meeting that was held on 19 December 2016. To propose a draft of this policy, a drug policy formulation committee and sub-committee were constituted in 2011⁵. The sub-committee has analyzed meticulously the problems and prospects of the country's pharmaceutical sector, discussed with many professional experts and leaders of this sector, gathered opinion from all stakeholders and incorporated important suggestions from the public. Thus this drug policy has turned to be both pro-industry and pro-people.

Essential drug list (EDL)

To protect public health effectively and to deal with emergency need of the majority of the people, separate EDL for Allopathic, Ayurvedic, Unani and Homeopathic-Biochemic systems of medicines have been prepared. The quantity of drugs in the Essential Drug List (Allopathic) is 285 (versus 150 in the drug policy of 1982 with 56 in the Supplementary List), the number of medicines in the Essential Drug List (Ayurvedic) is 100, the quantity of drugs in the Essential Drug List (Unani) is 223 and the quantity of drugs in the Essential Drug List (Homeopathic) is 370.

All the drugs included in this list must be available throughout the country so that people even from remote corners can get an easy access to these drugs. After every 2 years, all these lists will be updated from time to time. Regular updating and inclusion of more drugs in this list will help us to get patent waiver of drugs on public health issue beyond 2033.

Regulatory system

The Directorate General of Drug Administration (DGDA), Ministry of Health

Table 1. List of essential antibiotics surveyed

S No.	Beta Lactam antibiotics	Dosage form taken to check Availability	Dosage form taken to check Affordability and price
1	Amoxicillin	Capsule/Dry Syrup /Injection	Capsule 250mg
2	Ampicillin	Capsule/Dry Syrup /Injection	Capsule 250mg
3	Phenoxymethyl Penicillin	Tablet/Syrup	Tablet 250mg
4	Benzathine Penicillin	Injection	Injection 12 lac unit/vial
5	Flucloxacillin	Capsule/Syrup/Injection	Capsule 250mg
6	Procaine Penicillin	Injection	Injection 4 lac unit/vial
7	Cephadrine	Capsule/Syrup/Injection	Capsule 250mg
8	Cephalexin	Capsule/Tablet/Syrup	Cap 250mg
9	Benzyl Penicillin	Injection	Injection 5 lac unit/vial
10	Cloxacillin	Capsule/Syrup/Injection	Capsule 500mg
11	Amoxiclav(Amoxicillin + Clavulanic acid)	Tablet/Capsules/Dry Syrup/Injection	Tablet (250mg + 125mg)
	Other antibacterials		
12	Erythromycin	Tablet/Oral Suspension /Injection	Tablet 250mg
13	Chloramphenicol	Cap/Eye/Ear Drops/Ointment	Capsule 250mg
14	Doxycycline	Capsule	Capsule 100mg
15	Co-Trimoxazole (Trimethoprim + Sulfamethoxazole)	Tablet/Suspension	Tablet (800mg + 160mg)
16	Metronidazole	Tablet/Oral Liquid/Injection	Tablet 400mg
17	Tetracycline HCl	Capsule/Injection	Capsule 250mg
18	Nalidixic Acid	Tablet/Syrup	Tablet 500mg

and Family Welfare, is the National Regulatory Authority for drugs in Bangladesh. The DGDA oversees and implements all Drug laws in the country and guides all activities related to import, purchase of raw and packaging materials,

manufacture and import of finished drugs, export, sales and price fixation, etc. Currently there are 28,734 brands of medicine products and a total of 269 drug manufacturing companies ⁶.

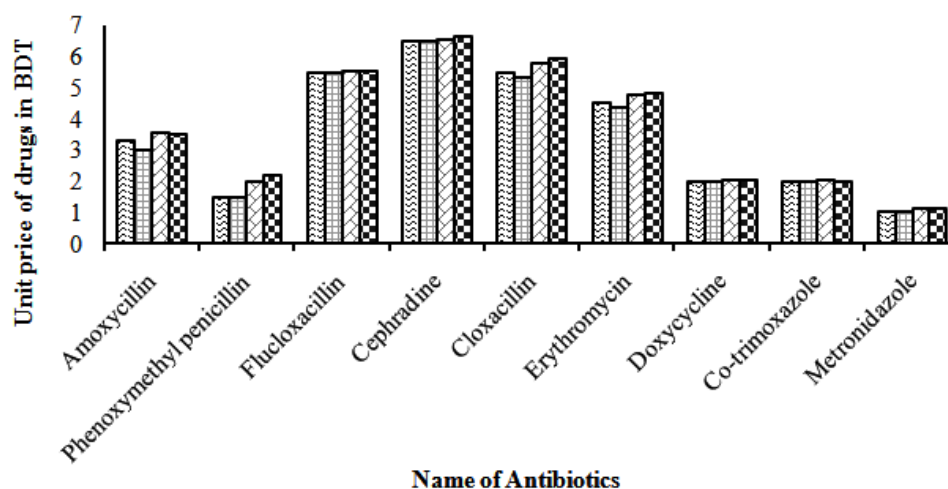






Fig. 1. Prices of some selected Essential Antibiotics of different years. Here,  = Year 2003,  = Year 2006,  = Year 2015 &  = Year 2019.

Table 2. Median unit price of medicines in different years

Medicines	Strength	Dosage form	Price in 2003	Price in 2006	Price in 2015	Price in 2019
Amoxicillin	250mg	Capsule	3.29	3.02	3.54	3.51
Ampicillin	250mg	Capsule	2.51	2.5	3.25	3.25
Benzathine Penicillin	12 lac units/vial	Injection	23.56	23.12	24.98	24.21
Flucloxacillin	250mg	Capsule	5.5	5.5	5.52	5.52
Procaine Penicillin	4 lac units/vial	Injection	6.81	7.6	14.05	10
Cephadrine	250mg	Capsule	6.5	6.5	6.525	6.65
Cephalexin	250mg	Capsule	6.285	6.5	6.575	6.5
Benzyl Penicillin	5 lac units/vial	Injection	6.365	6.36	11.29	8.76
Cloxacillin	500mg	Capsule	5.5	5.355	5.8	5.92
Amoxiclav (Amoxicillin + Clavulanic acid)	250mg+ 125mg	Tablet	20.22	16.25	16.57	20
Erythromycin	250mg	Tablet	4.5	4.35	4.75	4.82
Chloramphenicol	250mg	Capsule	2.5	2.35	2.5	2.5
Doxycycline	100mg	Capsule	2	2	2.03	2.06
Co-Trimoxazole (Trimethoprim + Sulfamethoxazole)	800mg + 160mg	Tablet	2	2	2.02	2.01
Metronidazole	400mg	Tablet	1.01	1.01	1.13	1.14
Tetracycline	250mg	Capsule	1.01	1	1.1	1.3
Nalidixic Acid	500mg	Tablet	3.85	3.87	4.87	4.03

Table 3. Statistical hypothesis testing

Paired t-test	Year 2003 vs Year 2006	Year 2003 vs Year 2015	Year 2003 vs Year 2019	Year 2006 vs Year 2015	Year 2006 vs Year 2019	Year 2015 vs Year 2019
p-value	Can't reject Null; p value= 0.325> $\alpha=0.05$	Can't reject Null; P value=0.168> $\alpha=.05$	Might reject Null; p-value =0.02< $\alpha=0.05$	Might reject null; pvalue =0.032< $\alpha=0.05$	Might reject Null; p value=0.007< $\alpha=0.05$	Can't reject null p value=0.510> $\alpha=0.05$
Result	Price difference not statistically significant	Price difference not statistically significant	Significant Price difference exist	Significant Price difference exist	Significant Price difference exist	Price difference not statistically significant

Methodology

With the help of the WHO/HAI methodology, we analyzed the availability, affordability and prices of 18 essential antibiotics. Availability of 18 essential medicines was obtained from 25 private pharmacies (Model pharmacies and general medicine stores). The medicine shops were located in different regions of the Dhaka Metropolitan City.

The prices of 18 essential medicines were also examined. The prices of drug were compared with international reference prices (IRPs). A comparative study on variation of prices across years was also done. A comparative statistical analysis among prices of different years was done by using SPSS statistic software. The local unit prices were collected from Bangladesh National Formulary which is the directory for all drugs produced locally and marketed in Bangladesh 7. International reference prices were utilized to compare national prices with the international standard.

The WHO/HAI methodology also evaluates the affordability of medicines, expressed as the number of day's salary needed by the lowest paid unskilled government laborer to buy a full-course of treatment. To estimate what drug prices mean in terms of affordability for mass people, some normal treatment costs were measured and compared with the salary of the lowest-paid unskilled laborer, which was 8000 Bangladeshi Taka per month⁸. All prices were converted to United States Dollar (USD) using the exchange rate on 30.06.2015 (\$1 USD = 77.83 Bangladeshi Taka)⁹. The international prices of 2015 were used as reference unit prices.

Survey medicines

A total of 18 essential antibiotics were selected from the Essential drug list of Allopathic drugs published by Directorate General of Drug Administration. All essential antibiotics were dose and dosage-form specific. The surveyed essential antibiotics were shown in Table 1. All surveyed essential antibiotics are generally used and have an available IRP.

Price component

Prices were obtained from BDNF-2, BDNF-3, BDNF-4 and DGDA of year 2003, 2006, 2015 and 2019, respectively. Essential antibiotics prices of 2015 according to BDNF 4

were then compared with the MSH 2015 IRPs. The drug prices were compared with international reference prices (IRPs). A comparative study on prices variation across years was also done. To ease international comparisons, medicine-specific median price ratios (MPR) were estimated when prices were available from at least four facilities. The MPR refers to the ratio of a medicine's local median unit price as compared to the 2015 MSH international median unit reference price.

Availability of essential antibiotics

The availability of essential antibiotics was expressed in two ways. One was the national availability of medicines which was calculated by counting the number of manufacturer in the country. The manufacturer numbers were collected from Bangladesh National Formulary^{7, 10, 11, 12}. Medicine availability was collected for different years as in 2001, 2003, 2006, 2015 and 2019. The data for the year of 2019 were collected from DGDA website.

Our study investigated the availability of essential antibiotics across Model pharmacies and general retail stores. The availability of medicine in retail medicine shops was expressed as percentage to the number of sites on day of data

collection. Only those medicines were considered available which were present at the time of data collection. Availability of 18 essential medicines were obtained from 25 private pharmacies (Model pharmacies and general medicine stores) and a comparison of mean percentage availability between 10 Model pharmacies and 15 General medicine stores were also studied using WHO/HAI methodology.

Affordability of essential antibiotics

The affordability of medicine was estimated as the number of days' wages that the lowest paid unskilled laborer would have to give for a standard treatment. As the government hospitals provide essential antibiotics to the patients free of cost, only the private sector medicine price was considered. The most common disease conditions were taken as standard for treatment approaches.

RESULTS AND DISCUSSION

The data for each medicine were collected from different sites and national formularies. Then the data were utilized in the program of MS Excel Workbook, given by the WHO/HAI. To avoid errors, data were checked and re-entered

Table 4. Price variation of essential antibiotics given in percentage across years

Medicine	Strength	Dosage form	Standard Price Year 2003	Price increased Or decreased in Percentage		
				Year 2006	Year 2015	Year 2019
Amoxicillin	250mg	Capsule	3.295	-8.34%(3.02)	7.43% (3.54)	6.52%(3.51)
Ampicillin	250mg	Capsule	2.515	-0.6%(2.5)	29.2%(3.25)	29.2%(3.25)
Phenoxymethyl penicillin	250mg	Tablet	1.47	0%(1.47)	35%(1.985)	49.6%(2.2)
Benzathine Penicillin	12 lac units/vial	Injection	23.56	-1.8%(23.12)	6%(24.98)	2.7%(24.21)
Flucloxacillin	250mg	Capsule	5.5	0%(5.5)	0.36%(5.52)	0.36%(5.52)
Procaine Penicillin	4 lac units/vial	Injection	6.815	11.5%(7.6)	106%(14.05)	46.7%(10)
Cephadrine	250mg	Capsule	6.5	0%(6.5)	0.38%(6.525)	2.3%(6.65)
Cephalexin	250mg	Capsule	6.285	3.4%(6.5)	4.6%(6.575)	3.4%(6.5)
Benzyl Penicillin	5 lac units/vial	Injection	6.365	0%(6.365)	77%(11.29)	37.7%(8.765)
Cloxacillin	500mg	Capsule	5.5	-2.6%(5.355)	5.4%(5.8)	7.6%(5.92)
Amoxiclav	250mg	Tablet	20.22	-19.6%(16.2)	-18%(16.57)	-1%(20)
Erythromycin	250mg	Tablet	4.5	-3.3%(4.35)	5.5%(4.75)	7.2%(4.825)
Chloramphenicol	250mg	Capsule	2.5	-6%(2.35)	0%(2.5)	0%(2.5)
Doxycycline	100mg	Capsule	2	0%(2)	1.5%(2.03)	3%(2.06)
Co-Trimoxazole	800mg + 160mg	Tablet	2	0%(2)	1%(2.02)	0.25%(2.01)
Metronidazole	400mg	Tablet	1.01	0%(1.01)	11.8%(1.13)	12.8%(1.14)
Tetracycline	250mg	Capsule	1.01	-0.9%(1)	8.9%(1.1)	28.7%(1.3)
Nalidixic Acid	500mg	Tablet	3.855	0.39%(3.87)	26%(4.87)	4.5%(4.03)

into the program. For a comparative study, prices of medicines of different years were collected. The drug unit price collected from the facility survey were entered into the MS Excel-based Workbook, followed by automated and manual

error-checking, and built-in automated analysis feature of the workbook. A comparative statistical

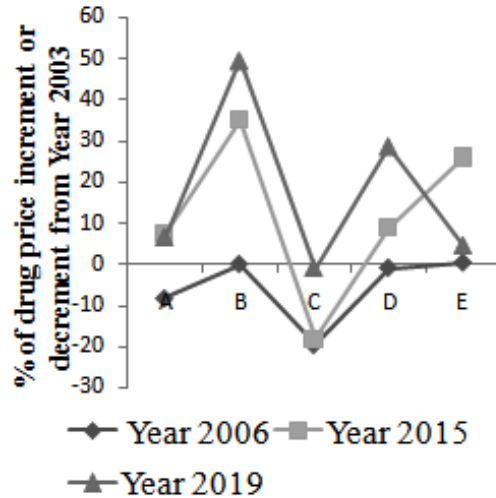
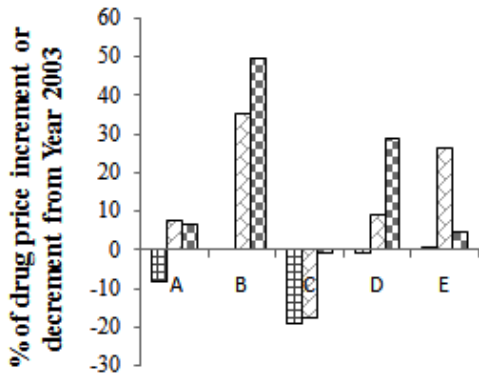


Fig 2a. In column chart Price variation in percentage of selected antibiotics across years taking Year 2003 (BDNF-2) drug price as standard

Fig 2b. In line chart Price variation in percentage of selected antibiotics across years taking Year 2003 (BDNF-2) drug price as standard

Here, = Year 2006, = Year 2015 & = Year 2019.

A=Amoxicillin Cap 250 mg B=Phenoxymethyl Penicillin Tab 250mg C=Amoxiclav Tab 250 mg D=Tetracycline Cap 250 mg E=Nalidixic Acid Tab 500 mg.

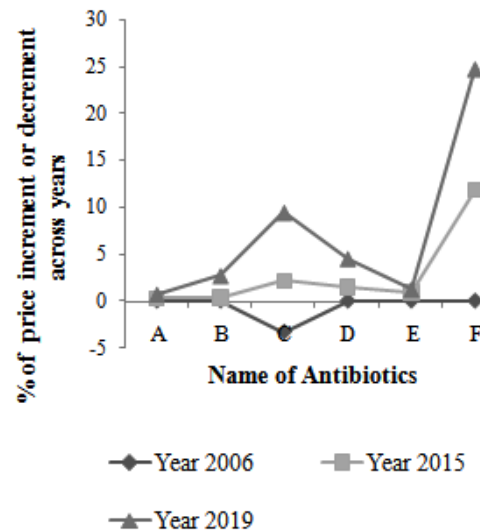
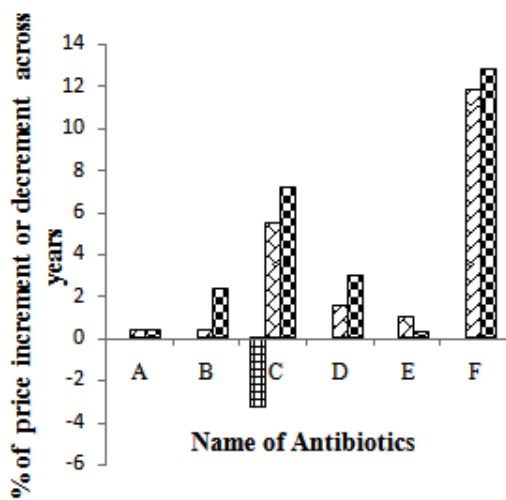


Fig. 3a. Price variation of selected antibiotics across years from year 2003. Drug price of year 2003 was taken as standard

Fig. 3b. Price variation of selected antibiotics across years from year 2003. Drug price of year 2003 was taken as standard

Here, = Year 2006, = Year 2015 & = Year 2019.

A= Flucloxacillin capsule 250mg B = cephradine capsule 250mg C= Erythromycin Tablet 250mg D= Doxycycline Capsule 250mg E= Co-trimoxazole tablet 800mg + 160mg F= Metronidazole Tablet 400mg.

analysis among prices of different years was done by using SPSS statistical software.

Price of medicines

The prices of selected medicines (Shown in Table 1) of different years (2003, 2006, 2015 and 2019) were collected and listed (Shown in Table 2). The medicine unit prices gathered from the facility survey were placed into the MS Excel-based Workbook. A comparative statistical analysis among prices of different years was done by using SPSS statistical software (Shown in Table 3). There are some medicines of which prices changed dramatically. Sometimes prices increased and sometime remained almost the same.

Figure 1 showed that the Median unit price of Amoxicillin Capsule (250 mg) was Tk. 3.29 in 2003, 3.02 in 2006, 3.54 in 2015 and 3.51 in 2019, respectively; that of Phenoxymethyl Penicillin Tablet (250 mg) was Tk. 1.47 in 2003, 1.46 in 2006, 1.98 in 2015 and 2.2 in 2019, respectively; that of Flucloxacillin Capsule (250 mg) was Tk. 5.5 in

2003, 5.5 in 2006, 5.52 in 2015 and 5.52 in 2019, respectively; that of Cephadrine Capsule (250 mg) was Tk. 6.5 in 2003, 6.5 in 2006, 6.52 in 2015 and 6.65 in 2019, respectively; that of Cloxacillin Capsule (500 mg) was Tk. 5.5 in 2003, 5.35 in 2006, 5.8 in 2015 and 5.92 in 2019, respectively; that of Erythromycin Tablet (250 mg) Tk. 4.5 in 2003, 4.35 in 2006, 4.75 in 2015 and 4.82 in 2019, respectively; that of Doxycycline Capsule (100 mg) was Tk. 2.00 in 2003, 2.00 in 2006, 2.03 in 2015 and 2.06 in 2019, respectively; that of Co-trimoxazole Tablet (800mg+160 mg) was Tk. 2.00 in 2003, 2 in 2006, 2.02 in 2015 and 2.00 in 2019, respectively; that of Metronidazole Tablet (400 mg) Tk. 1.01 in 2003, 1.01 in 2006, 1.13 in 2015 and 1.14 in 2019, respectively. Comparison between year 2003 and 2006

Medicines prices from year 2003 to 2006 were not changed much. Median prices of maximum medicine decreased in 2006 compared to year 2003. This difference of prices between year

Table 5. Median Price Ratio(MPR) of surveyed essential antibiotics

Medicines	Strength	Dosages form	Median international reference unit price (USD)	Median local unit price (USD)		Median price ratio (MRP)	
				2015	2019	2015	2019
Amoxicillin	250mg	Capsule	0.0227	0.0455	0.042	2.00	1.85
Ampicillin	250mg	Capsule	0.0163(S)	0.0417	0.039	2.56	2.39
Phenoxymethyl penicillin	250mg	Tablet	0.0388	0.0255	0.026	0.66	0.67
Benzathine Penicillin	12 lac units/vial	Injection	0.1809	0.321	0.29	1.77	1.6
Flucloxacillin	250mg	Capsule	0.0403	0.0709	0.066	1.76	1.64
Procaine Penicillin	4 lac units/vial	Injection	0.2951	0.1806	0.119	0.61	0.40
Cephadrine	250mg	Capsule		0.08383	0.079		
Cephalexin	250mg	Capsule	0.0475	0.08453	0.078	1.78	1.64
Benzyl Penicillin	5 lac units/vial	Injection	0.1224	0.1451	0.105	1.18	0.86
Cloxacillin	500mg	Capsule	0.0566	0.0745	0.071	1.32	1.25
Amoxiclav(Amoxicillin + Clavulanic acid)	250mg + 125mg	Tablet	0.1476 (S)	0.2130	0.239	1.44	1.62
Erythromycin	250mg	Tablet	0.045	0.0610	0.058	1.35	1.28
Chloramphenicol	250mg	Capsule	0.09	0.0321	0.03	0.36	0.33
Doxycycline	100mg	Capsule	0.0192	0.0261	0.025	1.36	1.30
Co-Trimoxazole (Trimethoprim + Sulfamethoxazole)	800mg + 160mg	Tablet	0.0314	0.0259	0.024	0.82	0.76
Metronidazole	400mg	Tablet	0.0157	0.0145	0.0136	0.92	0.83
Tetracycline	250mg	Capsule	0.0222	0.0141	0.016	0.63	0.67
Nalidixic Acid	500mg	Tablet	0.0435	0.0626	0.048	1.44	1.1

•S= Supplier price [As Buyer price not found]

2003 and year 2006 was not statistically significant (p value = 0.325).

Comparison between year 2003 and 2015

Median prices of maximum medicine increased in 2015 moderately compared to year 2003. This difference of prices between year 2003 and year 2015 was not statistically significant (p value = 0.168).

Comparison between year 2003 and 2019

Median prices of selected medicines increased in 2019 much compared to year 2003. This difference of prices between year 2003 and year 2019 was statistically significant (p value = 0.020).

Comparison between year 2006 and 2015

Median prices of selected medicines increased in 2015 much compared to year 2006. This difference of prices between year 2003 and year 2015 was statistically significant (p value = 0.032).

Comparison between year 2006 and 2019

Median prices of selected medicines increased in 2019 greatly compared to year 2006. This difference of prices between year 2003 and

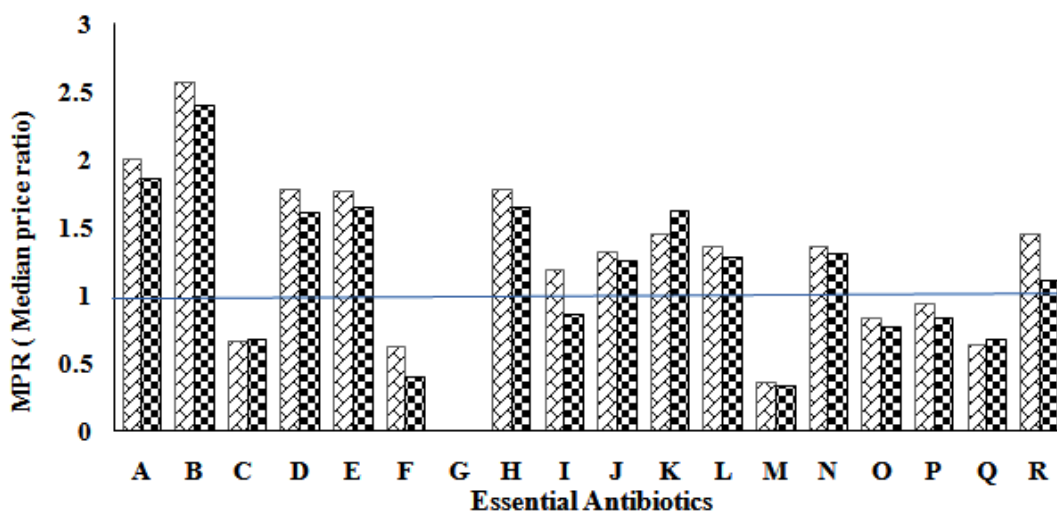
year 2019 was statistically significant (p value = 0.007).



Comparison between year 2015 and 2019

Median prices of selected medicines increased in 2019 greatly compared to year 2015. This difference of prices between year 2015 and year 2019 was not statistically significant (p value = 0.510).

Figure 2a showed that the Median unit price of Amoxicillin Capsule (250 mg) decreased 8.34% from 2003 to 2006, increased 7.43% from 2003 to 2015, and 6.52% from 2001 to 2019; that of Phenoxymethyl Penicillin Tab (250 mg) increased 0% from 2003 to 2006, 35% from 2003 to 2015 and 49.6% from 2003 to 2019; that of Amoxiclav Tablet (250 mg) decreased 19.6% from 2003 to 2006, 18% from 2003 to 2015 and 1% from 2001 to 2019; that of Tetracycline Capsule (250 mg) decreased 0.9% from 2003 to 2006, 8.9% from 2003 to 2015 and 28.7% from 2003 to 2019; that of Nalidixic Acid Tablet (500 mg) increased 0.389% from 2003 to 2006, 26% from 2003 to 2015 and 4.5% from 2003 to 2019, respectively.

A plot was drawn using selected antibiotics showed a great deviation in price over years (Figure 3(a), 3(b)).



Here,  = Year 2015 &  = Year 2019.

A=Amoxicillin B=Ampicillin C=Phenoxymethyl Penicillin D=Benzathine Penicillin E= Flucloxacillin F= Procaine Penicillin G=Cephadrine H=Cephalexin I= Benzyl Penicillin J= Cloxacillin K=Amoxiclav L=Erythromycin M= Chloramphenicol N=Doxycycline O=Co-Trimoxazole P= Metronidazole Q=Tetracycline R=Nalidixic Acid.

Fig. 4. Median Price Ratio (MPR) of selected essential antibiotics

Figure 3a showed that the Median unit price of Flucloxacillin Capsule 250 mg increased 0% from 2003 to 2006, increased 0.36% from 2003 to 2015 and 0.36% from 2001 to 2019; that of Cephadrine Capsule 250 mg increased 0% from 2003 to 2006, 0.38% from 2003 to 2015 and 2.3% from 2003 to 2019 ; that of Erythromycin Tablet 250 mg decreased 3.3% from 2003 to 2006, 5.5% from 2003 to 2015 and 7.2% from 2001 to 2019; that of Doxycycline Capsule 250 mg increased 0% from 2003 to 2006, 1.5% from 2003 to 2015 and 3% from 2003 to 2019; that of Co-trimoxazole Tablet 800 mg+160 mg increased 0% from 2003 to 2006, 1% from 2003 to 2015 and 0.25% from 2003 to 2019; that of Metronidazole Tablet 400 mg increased 0% from 2003 to 2006, 11.8% from 2003 to 2015 and 12.8% from 2003 to 2019, respectively.

Median Price Ratio (MPR)

Median Price Ratio (MPR) of medicines was calculated to observe how many times greater or lesser the price of local medicines to international reference unit prices. The formula for calculating MPR is given below –

$$\text{Median Price Ratio (MPR)} = \frac{\text{Median local unit price}}{\text{International reference unit price}}$$

The medicine prices of year 2015 and 2019 were converted to US Dollar using the exchange rate on 30.06.2015 (\$1 USD = 77.83 Bangladeshi Taka) and 28.01.2019 (\$1 USD= 83.4643 BDT), respectively. The international prices of 2015 were used as reference unit prices.

Figure 4 showed that the Median Price Ratio (MPR) of Amoxicillin was 2.00 and 1.85 in 2015 and 2019, respectively; that of Ampicillin was 2.56 and 2.39 in 2015 and 2019, respectively; that of Phenoxymethyl Penicillin was 0.66 and 0.67 in 2015 and 2019, respectively; that of Benzathine Penicillin was 1.77 and 1.6 in 2015 and 2019, respectively; that of Flucloxacillin was 1.76 and 1.64 in 2015 and 2019, respectively; that of Procaine Penicillin was 0.61 and 0.4 in 2015 and 2019, respectively; that of Cephadrine was not found; that of Cephalexin was 1.78 and 1.64 in 2015 and 2019, respectively; that of Benzyl Penicillin was 1.2 and 0.86 in 2015 and 2019,

Table 6. Availability and Market growth of essential antibiotics

Medicines	Dosages Form	No. of manufacturers in different year				
		2001	2003	2006	2015	2019
Amoxicillin	Capsule/Dry Syrup /Injection	10	75	70	45	69
Ampicillin	Capsule/Dry Syrup /Injection	10	11	9	6	6
PhenoxymethylPenicillin	Tablet/Syrup	10	15	17	10	16
Benzathine penicillin	Injection	7	4	5	2	6
Flucloxacillin	Capsule/Syrup/Injection	10	46	57	49	70
Procaine penicillin	Injection	4	2	3	3	4
Cephadrine	Capsule/Syrup/Injection	10	54	58	57	79
Cefalexin	Capsule/Tablet/Syrup	11	39	30	8	20
Benzyl penicillin	Injection	3	3	2	1	4
Cloxacillin	Capsule/Syrup/Injection	10	30	26	14	16
Amoxiclav (Amoxicillin + Clavulanic acid)	Tablet/Capsules/ Dry Syrup/Injection	8	4	4	8	14
Erythromycin	Tablet/Oral Suspension /Injection	10	27	40	40	50
Chloramphenicol	Eye/Ear Drops/Ointment	4	5	4	21	25
Doxycycline	Capsule	10	47	46	25	40
Co-trimoxazole (Trimethoprim + Sulfamethoxazole)	Tablet/Suspension	9	69	60	33	32
Metronidazole	Tablet/Oral Liquid/Injection	11	77	70	44	80
Tetracycline	Capsule/Injection	10	37	34	14	26
Nalidixic acid	Tablet/Syrup	10	12	11	4	9

respectively; that of Cloxacillin was 1.32 and 1.25 in 2015 and 2019, respectively; that of Amoxiclav was 1.44 and 1.62 in 2015 and 2019, respectively; that of Erythromycin was 1.36 and 1.28 in 2015 and 2019, respectively; that of Chloramphenicol was 0.36 and 0.33 in 2015 and 2019, respectively; that of Doxycycline was 1.36 and 1.3 in 2015 and 2019, respectively; that of Co-Trimoxazole was 0.82 and 0.76 in 2015 and 2019, respectively; that of Metronidazole was 0.93 and 0.83 in 2015 and 2019, respectively; that of Tetracycline was 0.64 and 0.67 in 2015 and 2019, respectively; that of Nalidixic Acid was 1.44 and 1.1 in 2015 and 2019, respectively.

Availability of medicines

For assessing medicine availability, manufacturers of each medicine were counted. This gave the national availability of the medicines. By collecting data from different retail pharmacies, availability of medicines at regional level was determined. It is important to mention that the availability given in the results refers to all eighteen examined essential antibiotics. Only that antibiotics were seen at the time of data collection were termed as available.

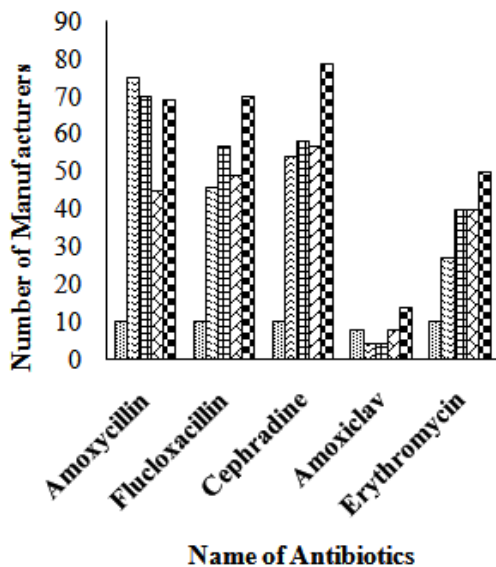


Fig. 5a. Manufacturers number of selected essential antibiotics across years

Here, [Pattern 1] =Year 2001, [Pattern 2] =Year 2003, [Pattern 3] = Year 2006, [Pattern 4] = Year 2015 & [Pattern 5] = Year 2019.

Figure 5a showed that the number of manufacturers of Amoxicillin was 10 in 2001, 75 in 2003, 70 in 2006, 45 in 2015 and 69 in 2019; that of Flucloxacillin was 10 in 2001, 46 in 2003, 57 in 2006, 49 in 2015 and 70 in 2019; that of Cephadrine was 10 in 2001, 54 in 2003, 58 in 2006, 57 in 2015 and 79 in 2019; that of Amoxiclav was 8 in 2001, 4 in 2003, 4 in 2006, 8 in 2015 and 14 in 2019; that of Erythromycin was 10 in 2001, 27 in 2003, 40 in 2006, 40 in 2015 and 50 in 2019, respectively. Here, =Year 2001, =Year 2003, = Year 2006, = Year 2015 & = Year 2019.

Figure 5b showed that the number of manufacturers of Amoxicillin increased 650% from 2001 to 2003, 600% from 2001 to 2006, 350% from 2001 to 2015 and 590% from 2001 to 2019; that of Flucloxacillin increased 360% from 2001 to 2003, 470% from 2001 to 2006, 390% from 2001 to 2015 and 600% from 2001 to 2019; that of Cephadrine increased 440% from 2001 to 2003, 480% from 2001 to 2006, 470% from 2001 to 2015 and 690% from 2001 to 2019; that of Amoxiclav decreased 50% from 2001 to 2003, 50% from 2001 to 2006,

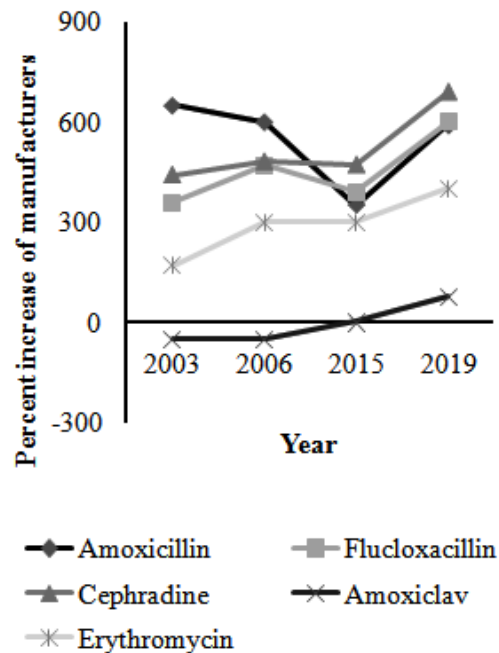


Fig. 5b. Percent increase of manufacturers across years

increased 0% from 2001 to 2015 and 75% from 2001 to 2019; that of Erythromycin increased 170% from 2001 to 2003, 300% from 2001 to 2006, 300%

from 2001 to 2015 and 400% from 2001 to 2019, respectively.

A total of 25 retail pharmacies were

Table 7. Availability of generic equivalent medicines in retail pharmacies.

Medicine	Dosages Form	Availability in percentage(%)	
		Model Pharmacy (n=10)	General medicine store(n=15)
Amoxicillin	Capsule/Dry Syrup /Injection	100%	93.33%
Ampicillin	Capsule/Dry Syrup /Injection	70%	26.66%
PhenoxymethylPenicillin	Tablet/Syrup	90%	53.33%
Benzythine penicillin	Injection	80%	33.33%
Flucloxacillin	Capsule/Syrup/Injection	100%	86.66%
Procaine penicillin	Injection	20%	0%
Cephadrine	Capsule/Syrup/Injection	100%	80%
Cephalexin	Capsule/Tablet/Syrup	60%	6.66%
Benzyl penicillin	Injection	30%	6.66%
Cloxacillin	Capsule/Syrup/Injection	90%	26.66%
Amoxiclav(Amoxicillin + Clavulanic acid)	Tablet/Capsules/ Dry Syrup/Injection	100%	86.66%
Erythromycin	Tablet/Oral Suspension /Injection	100%	66.66%
Chloramphenicol	Eye/Ear Drops/Ointment	70%	40%
Doxycycline	Capsule	90%	66.66%
Co-trimoxazole (Amoxicillin + Clavulanic acid)	Tablet/Suspension	100%	46.66%
Metronidazole	Tablet/Oral Liquid/Injection	100%	86.66%
Tetracycline	Capsule/Injection	100%	46.66%
Nalidixic acid	Tablet/Syrup	50%	33.33%

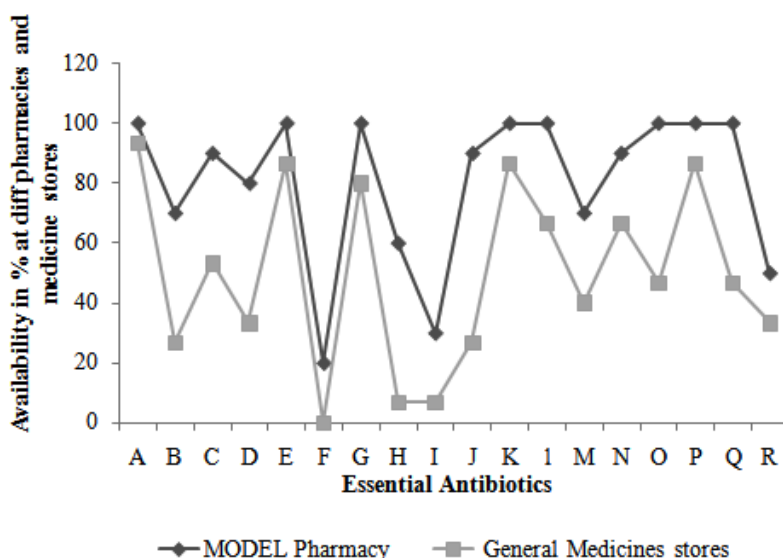


Fig. 6. Availability of selected essential antibiotics at Dhaka Metropolitan city in Bangladesh. A=Amoxicillin B=Ampicillin C=Phenoxymethyl Penicillin D=Benzathine Penicillin E= Flucloxacillin F= Procaine Penicillin G=Cephadrine H=Cephalexin I=Benzyl Penicillin J=Cloxacillin K=Amoxiclav L=Erythromycin M= Chloramphenicol N=Doxycycline O=Co-Trimoxazole P= Metronidazole Q=Tetracycline R=Nalidixic Acid

inspected to gather information about the described medicines. Availability of a medicine was ensured when one outlet had the medicine of any dose and dosage form on the time of data collection. However, data were collected from different types of retail pharmacies- large, small; medicine shop, model pharmacy; medicine stores located near the both government and non-government hospitals. The retail shops were located in different regions of the Dhaka Metropolitan City. In inspected retail shops, the essential antibiotics were poorly available in general medicine stores as compared to the Model pharmacies. So availability is higher in Model pharmacies than General medicine stores.

Figure 6 showed that the availability of Amoxicillin was 100% and 93.3% in Model pharmacies and General medicine stores respectively; that of Ampicillin was 70% and 26% in Model pharmacies and General medicine stores respectively; that of Phenoxymethyl Penicillin was 90% and 53% in Model pharmacies and General medicine stores respectively; that of Benzathine Penicillin was 80% and 33.3% in

Model pharmacies and General medicine stores respectively; that of Flucloxacillin was 100% and 86% in Model pharmacies and General medicine stores respectively; that of Procaine Penicillin was 20% and 0% in Model pharmacies and General medicine stores respectively; that of Cephadrine was 100% and 80% in Model pharmacies and General medicine stores, respectively ; that of Cephalexin was 60% and 7% in Model pharmacies and General medicine stores, respectively; that of Benzyl Penicillin was 30% and 7% in Model pharmacies and General medicine stores, respectively; that of Cloxacillin was 90% and 26% in Model pharmacies and General medicine stores, respectively; that of Amoxiclav was 100% and 86% in Model pharmacies and General medicine stores, respectively; that of Erythromycin was 100% and 66% in Model pharmacies and General medicine stores respectively; that of Chloramphenicol was 70% and 40% in Model pharmacies and General medicine stores, respectively; that of Doxycycline was 90% and 66% in Model pharmacies and General medicine stores, respectively; that

Table 8. Prices per regimens of treatment with different essential antibiotics

Medicine	Strength	Course of treatment	No. of units per treatment	Median price pertab/vial	Price per course of treatment	Number of days' wages
Amoxicillin	Cap 250mg	6 Cap/day, 7 days	42	3.51	147.42	0.553
Ampicillin	Cap 250mg	6 Cap/day,7 days	42	3.25	136.5	0.512
Phenoxymethyl-penicillin	Tab 250mg	8 tab/day, 7 days	56	2.2	123.2	0.462
Benzathine penicillin	Inj12 lac unit/vial	2 Inj/week,3 weeks	6	24.21	145.26	0.545
Flucloxacillin	Cap 250mg	6 Cap/day, 7 days	42	5.52	231.84	0.87
Procaine penicillin	Inj4 lac unit/vial	2vial/day, 10 days	20	10	200	0.75
Cephadrine	Cap 250mg	8 Cap/day, 7 days	56	6.65	372.4	1.4
Cephalexin	Cap 250mg	8 Cap/day, 7 days	56	6.5	364	1.36
Benzyl penicillin	Inj 5lac unit/vial	4 vial/day, 5 days	20	8.765	175.3	0.66
Cloxacillin	Cap 500mg	4 cap/day, 7 days	28	5.92	165.76	0.6216
Amoxiclav (Amoxicillin + Clavulanic acid)	Tab 250mg+125mg	6 tab/day, 7 days	42	20	840	3.15
Erythromycin	Tab 250mg	8 tab/day, 7 days	56	4.825	270.2	1.01
Chloramphenicol	Cap 250mg	8 Cap/days,5 days	40	2.5	100	0.4
Doxycycline	Cap 100mg	2 Cap/day,7 days	14	2.06	28.84	0.11
Co-trimoxazole (Trimethoprim + Sulfamethoxazole)	Tab 800mg+160mg	2 Cap/day,7 days	14	2.005	28.07	0.105
Metronidazole	Tab 400mg	4 cap/day, 7 days	28	1.14	31.92	0.12
Tetracycline	Cap 250mg	8 Cap/day, 7 days	56	1.3	72.8	0.273
Nalidixic acid	Tab 500mg	8 Cap/day, 7 days	56	4.03	225.68	0.8463

of Co-Trimoxazole was 100% and 46% in Model pharmacies and General medicine stores respectively; that of Metronidazole was 100% and 86% in Model pharmacies and General medicine stores, respectively; that of Tetracycline was 100% and 46% in Model pharmacies and General medicine stores, respectively; that of Nalidixic Acid was 50% and 33.3% in Model pharmacies and General medicine stores, respectively.

Affordability of medicine

Medicine affordability was estimated by calculating the expenses of standard treatment to complete a full course (Shown in Table 7). The prices of medicines of 2019 were considered. The government of Bangladesh, on September 13, 2018 announced Tk. 8000 BDT as the minimum salary for Garment worker. The lowest monthly wage of unskilled people was considered as 8000 BDT. The economic condition of Bangladesh is also growing healthy. The per capita national income is also increasing every year. So the medicines are also becoming more affordable. The following table gives some idea about health and economic status of Bangladesh.

The number of day's salaries necessary to buy a course of treatment (shown in Table 8) was

estimated from the daily wages of the lowest-paid unskilled laborer (266.67 BDT).

DISCUSSION

In visited retail shops, the essential antibiotics were less available in general medicine stores as compared to the Model pharmacies. A comparative study on prices variation across years had shown a moderate increase in price. The median prices of surveyed antibiotics were obtained and a gross comparison was done that indicated % increase or decrease in price. In the study, the median price ratios of surveyed antibiotics ranged from 0.36-2.56 and 0.33-2.39 in Year 2015 and 2019, respectively. While observing the WHO target that patients should pay no more than four times the IRPs, we found that medicine prices were lower in the Bangladesh compared to IRPs. A medicine price survey in Bahrain during 2013 utilizing the WHO/HAI method, exhibited that patients were paying 34.78 and 13.85 times IRPs for innovator brands and lowest paid generics, respectively. Patients were paying 13.05 and 4.12 times IRPs for innovator brands and lowest paid generics, respectively during 2011 at Tatarstan

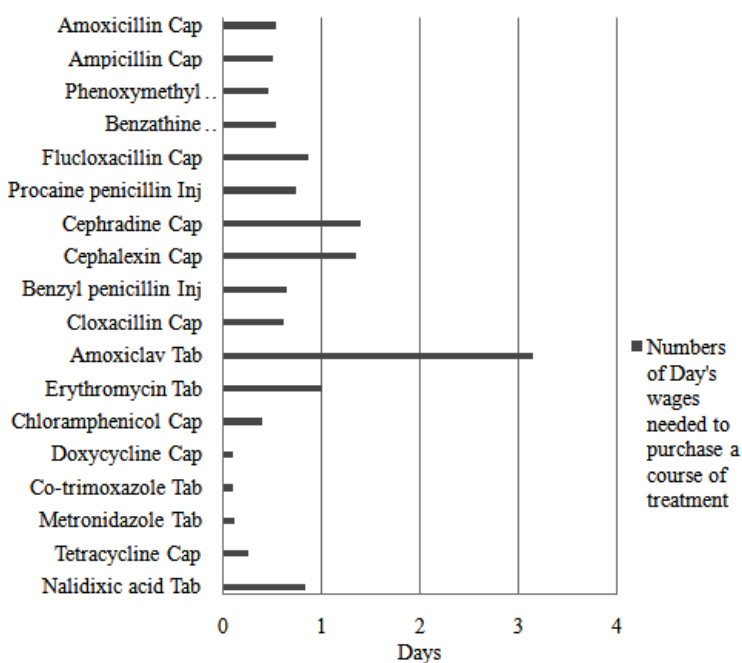


Fig. 7. Affordability of essential antibiotics in Bangladesh

Province of Russia. While patients were paying 61.44 and 17.33 times IRPs for innovator brands and lowest paid generics, respectively¹³, in a Caribbean country in 2010. Our findings gave the idea that the essential antibiotics were affordable in Bangladesh.

CONCLUSIONS

Medicine prices are not much higher than international reference prices. In comparison to the WHO target, medicine prices were considerably lower in the Bangladesh. We also observed a wide variation in terms of the MPR results for different antibiotics in our work. The prices for medicines included were near to WHO's target. The essential antibiotics were affordable. These data exhibit that the antibiotics targeted by the study have a high variation in prices. The reason for this variation may be due to fewer generics on the market and therefore they have a widespread availability in the first level health facilities, which may result in decreased prices relative to the international reference. Some treatments are affordable for families on a low income. This is especially true for essential medicine used in the treatment of different diseases. The numbers of manufacturers for several medicines have increased in a very rapid speed. Mostly used antibiotics manufacturers are increasing from the last consecutive years.

Based on the findings of the study, it is inferred that – (i) Investigating the availability of medicines in government hospitals and examining models that are able to provide good prices and availability at their hospital, (ii) Establishing a price regulation mechanism for essential medicines, (iii) Medicine price monitoring should be performed at regular interval. To more precisely control price and availability trends, prices must be monitored regularly and have the results made widely available, (iv) There are several medicines which are manufactured by only a few companies. As a result, the prices of those medicines remain very high in comparison to international reference prices. The government should be aware that essential medicines are manufactured by almost all company, (v) There should be a database for the prices of medicines of previous years so that one can easily compare the price changes among

years. This database should be available for mass people.

ACKNOWLEDGEMENT

We express our gratitude to the authority of Directorate General of Drug Administration (DGDA).

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