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Pharmacoeconomic Evaluation of Antimicrobial Therapy at a Secondary Health Facility in Minna, Northern Nigeria

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Abstract: In countries with depressed economy, there is a need for utmost economic consideration when choosing treatment options. The pharmacoeconomics of the prescribed antimicrobial drugs in general hospital, Minna, between January and December 2008 was studied retrospectively. The objective is to pharmacoeconomically evaluate the prescribed antimicrobials with a view to aid individuals and Government in choosing treatment options within limited resources. Two thousand one hundred and eighty (2,180) prescriptions were obtained from the outpatient medical record department using simple random sampling technique. One thousand, three hundred and eighty-four (1,384) prescriptions were excluded from the study because they did not contain antimicrobial drugs. Therefore, 796 prescriptions were used for the study. Information extracted included demographic data and rationally prescribed drugs.
Results showed that average number of drugs per prescription was 3.6. Quinolones were the highest prescribed 247(31%) while antituberculosis drugs were the least, accounting for 22(2.8%). Total cost of antimicrobials prescribed was found to be NGN652,38 (US $4,263) with quinolones accounting for the highest amount of NGN261,84 (US $1,711.38). Cost effectiveness analysis (CEA) for tuberculosis treatment revealed that Ethambutol was more cost effective than Rifampicin ($P<0.05$).
The study showed that antimicrobials were frequently prescribed; however, stocking of medications and cost of therapy should be thoroughly appraised for pharmacoeconomics justification.
Keywords: Pharmacoeconomics, Antimicrobials, Therapy, Quinolones, Ethambutol.
Running title: Pharmacoeconomics of antimicrobial therapy.

INTRODUCTION

Pharmacoeconomics is a specialized aspect of health economics which involves the use of economics principles and technique of analysis to ensure that scarce health care resources were used more efficiently[1].
Nigeria operates a three-tier health care system, the federal ministry of health (FMOH), state ministries of health (SMOH) and local governments' primary health care departments. These three tiers broadly have responsibility of tertiary, secondary, and primary health care respectively. Lack of clear roles of each of these tiers, leads to treatments overlap and neglect of essential service deliveries. However, with the services rendered through national health insurance scheme (NHIS), non-governmental organizations (NGOS) and managed care organizations (MCO), health care systems are taking new dimensions.
The health components of federal budget has increased in terms of budgetary allocation from NGN16 billion (1.7% of federal budget) in 1999 to NGN63.2 billion (6.4%) in 2002. However, the projected figure for 2006 was NGN106.904 billion, 5.6% of the total budget proposal which was a 40% increase in budgetary allocation over the 2002 [2].
Budgetary allocation in health sector is increasing as a result of cost increment, and because of the growing population that prompted new health policies. Subsequently, total health spending and per capital spending is increasing.
Spiraling cost have compelled health care payers to be conscious of their approach to purchasing[3]. In countries with depressed economy such as Nigeria where per capital income is low, there is a need for utmost consideration for cost containment measures[4,5,]. Pharmaceuticals are very important drivers of health care expenditure and major target of cost containment measures[6,7]. Drug budgets are easier to identify than the other cost as the component of a hospital budget. Pharmaceutical costs present variable costs that make them easier target for cost containment measure when compared to some fixed hospitals costs such as admission costs.
Medical, ethical and social concern about costs, and quality of care are causing health care practitioners to consider more comprehensive model for making medical decision. Sound clinical, financial and business skills will be required to meet the associated challenges. Interest in research of health care is increasing. Hospital and clinical Pharmacists find themselves ideally positioned to make significant contributions because of their broad educational background and practice in the three-tier health care systems. These have led to

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pharmacoeconomics[8] evaluations. Pharmacoeconomics evaluation of therapy is increasingly advocated especially in the developing countries such as Nigeria[9,10].

Pharmacoeconomics evaluation influences policy making and decision making thereby making an individual or a group of people change their behaviour because they are persuaded that a new course of action is a "better" one. "Better" simply means, in economic terms, a new course is more effective[11].

The main objective of this study is to establish cost effective treatment options involving antimicrobials pharmacoeconomically with the goal of providing and promoting pharmaceutical care

PATIENTS AND METHODS

This retrospective study was carried out at the General hospital, Minna, Niger State, Nigeria and involved outpatient case-notes, dispensed prescriptions, stop watch and calculator. In addition, stopwatch time-study in conjunction with standard cost accounting techniques was equally used.

The results were analyzed using Cost minimization analysis (CMA) and Cost effectiveness analysis (CEA).

Elderly patients who were prescribed antimicrobials in out – patient department were used for the study. Simple random sampling used involved studying the case notes of patients who met the inclusion criteria over a specified time interval, that is, patients who were prescribed antimicrobials as major drug therapy within the period covered in the study. Prescriptions examined were those dispensed in the months of January to December in 2008.

Two thousand, one hundred and eighty (2180) out-patient prescriptions were randomly selected out of which 796 that have antimicrobials as the main therapy were studied retrospectively. This is in addition to other relevant data such as patients' demographics and other rationally prescribed drugs.

The cost per defined daily dosage (DDD) of antimicrobial for each patient was calculated. DDD units are recommended standard by WHO for drug use analysis. One DDD represents the daily dosage of antimicrobial per day. Erythromycin, 1g per day in 4 divided doses[24] is one DDD. The total cost of drug for each visit was also calculated taking the DDD and the duration of therapy (DOT) into consideration.

The personnel costs were calculated by assuming the average time for 10 random observations for completion of tasks such as: pharmacist dispensing and drug administration by the staff nurse. The salary of health professionals was then determined from the accounts department of the hospital. The average was considered and the mean salary per minute computed using the formula below:

$$Mean\ salary/minute = \frac{Annual\ salary}{\frac{Hours}{week} \times No\ of\ weeks/Annum \times 60}$$

The respective number of visits to the hospital by the patients was also added together.

The transportation cost for each patient during the hospital visits within the year under review was computed by using the standard tariff of National Union of Road Transport Workers (NURTW) with the patient's destination obtained from the stated patients' address in the case notes.

Cost Minimization Analysis (CMA), a typical pharmacoeconomics methodology in which the outcome units is assumed to be equivalent among the comparative groups is the appropriate pharmacoeconomics tool used when there are documented claims of therapeutic equivalence.[28]

Statistical analysis was performed for more objective conclusion to be drawn. The students "t" test was used to determine values (mean) of cost/DDD of each antimicrobial (branded and generic). Chi-square test was used to compare the different treatment options.

Ethical approval was granted by the Hospital Management Board, Minna.

RESULTS

Table 1 shows the antimicrobial usage in General Hospital, Minna. The total number of prescriptions sampled was 2, 180 out of which 796 (36.5%) that contained antimicrobials were selected and studied. Table 2 shows the classification and total cost of prescribed antimicrobials with Penicillin accounting for 23.4% (₦ 56, 222.00), Cephalosporin 10.6% (₦80, 160.00), Quinolones 31% (₦22, 000.00), Antituberculosis and Aminoglycosides 2.8% (₦173, 560.00) and Macrolides, Tetracyclines and other antimicrobials accounting for 15% (₦652, 382.00).

TABLE 1: ANTIMICROBIAL USAGE IN GENERAL HOSPITAL, MINNA.

INSTITUTION	NO. OF PRESCRIPTION SAMPLED	PPAM	PROPORTION OF PPAM WITH MULTIPLE ANTIMIROBIAL PRESCRIPTION	AVERAGE NO. OF DRUG PER PRESCRIPTION		
				NOAM	OTHER DRUG	TOTAL
GHM	2,180	796(36.51)	17.20	1.56	2.04	3.6

NOPS – No of prescriptions sampled
PPAM – Percentage of prescription with antimicrobials
NOAM – No of antimicrobials.
GHM – General Hospital, Minna

Table 2: Classification and Total cost in Naira of Prescribed Antimicrobial

CLASS OF DRUG	FREQUENCY	PERCENT	TOTALCOST(NAIRA)
Penicillin	187	23.4	56,222 (367.46US Dollars)
Cephalosporin	84	10.6	80,160 (523.92 US Dollars)
Quinolones	247	31.0	261,840 (1,711.37 US Dollars)
Imidazoles	133	17.0	22,000 (143.79 US Dollars)
Antituberculosis & Aminoglycosides	22	2.8	58,600 (383.00 US Dollars)
Macrolides,Tetracyclines & others.	121	15.0	173,560 (1,134.38 US Dollars)
	Total	100.0	625,382 (4,263.92 US Dollars)

Fig. 1 Bar chart showing the gender distribution of patients prescribed antimicrobials

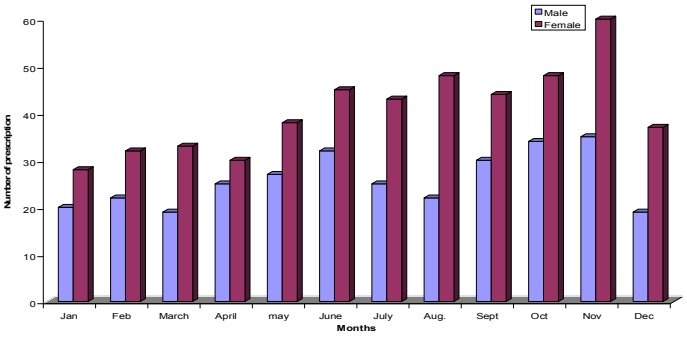

Table 3 shows cost per defined daily dose (DDD) of antimicrobials in General Hospital, Minna. The DDD of branded Augmentin Tab 625mg bid, Augmentin tab 375mg tid, Cefuroxime inj. 750mg bid, Ciprofloxacin tab 500mg bid and Co-trimoxazole tab 960mg bid are 400.00 naira, 225.00 naira, 1400.00 naira, 160.00 naira and 80.00 naira respectively while the DDD of their generic equivalent are 280.00 naira, 125.00 naira, 1000.00 naira, 70.00 naira and 8.00 naira respectively.

Table 4 shows the cost minimization analysis (CMA) of selected antimicrobials in branded and generic formulations. Branded Ciprofloxacin tabs 500mg bid, Co-trimoxazole tab 960mg bid and Augmentin tab 375mg tid are 160.00 naira, 80.00 naira and 225.00 naira mean cost/DDD while the mean cost/DDD of their generic equivalent are 70.00 naira, 8.00 naira and 125.00 naira respectively.

TABLE 3: COST PER DDD OF ANTIMICROBIALS IN GH MINNA

S/N	ANTIBIOTIC	DOSE (DDD)	MEAN COST/DDD (N) N = NAIRA DDD = DEFINED DAILY DOSE	
			Branded	Generic
1.	Ampicillin cap.	250mg qid	-	40±0
2..	Ampiclox cap	500mg qid	-	24±0
3.	Augmentin tab	625mg bid	400±0	280±0
4.	Augmentin tab	375mg tid	225±0	125±0
5.	Cefuroxime tab	250mg bid	-	100±0
6.	Cefuroxime inj.	750mg bid	1400±0	1000±0
7.	Cefotaxime inj.	1000mg bid	-	1000±0
8.	Ciprofioxacin tab.	500mg bid	160±0	70±0
9.	Cotrimoxazole tab.	960mg bid	80±0	8±0
10.	Doxycycline cap.	100mg bid	300±0	20±0
11.	Ethambutol tab.	400mg bid	-	12±0
12.	Erythromycin	500mg qid	160±0	100±0
13.	Gentamycin inj.	280mg o.d	-	30±0
14.	Griseofulvin tab.	500mg o.d	-	20±0
15.	Isoniazid tab.	300mg o.d	-	3±0
16.	Metronidazole tab.	400mg tid	-	12±0
17.	Nalidixic acid tab.	500mg qid	40±0	-
18.	Neomycin tab.	500mg qid	-	20±0
19.	Procaine penicillin	60mg o.d	-	20±0
20.	Rifampicin cap	600mg o.d	50±0	20±0
21.	Streptomycin inj.	1000mg o.d	-	10±0
22.	Benzathine penicillin inj.	2.4 iu	-	350±0

TABLE 4: COST/DDD OF SELECTED ANTIMICROBIALS FOR COST MINIMIZATION ANALYSIS (CMA) IN GENERAL HOSPITAL, MINNA.

S/N	ANTIMIROBIAL	DOSE(DDD)	MEAN COST/DEFINED DAILY DOSE (N)	
			Branded	Generic
1.	Ciprofloxacin tab	500mg bid	160±0	70±0
2.	Cotrimaxazole tab.	960mg bid	80±0	8±0
z3.	Augmentin tab.	375mg tid	225±0	125±0
4.	Erythromycin cap.	500mg qid	160±0	100±0
5.	Rifampicin cap.	600mg o.d	50±0	20±0
6.	Doxycycline cap.	100mg bid	300±0	20±0

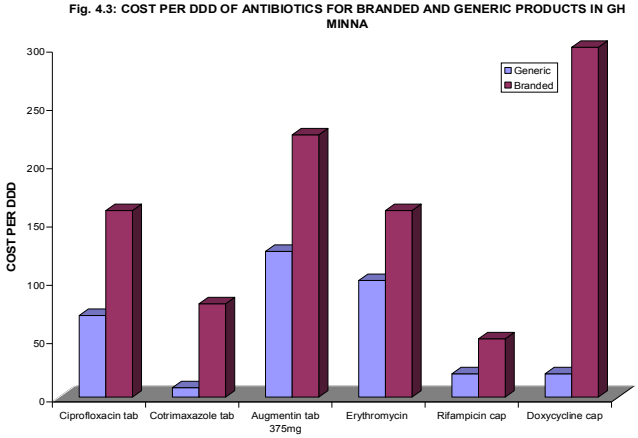

Fig. 2 Cost period of antibiotics for branded and generic products in Gh. Minna

Table 5 shows the effectiveness rating for antituberculosis drugs considering criteria such as spectrum of antituberculosis activity, pharmacokinetics, drug interactions and adverse drug reactions (ADR).

Rifampicin capsule was found to be equally effective as ethambutol tablet, in their spectrum of activity. Pharmacokinetically, Ethambutol was 70% more effective than Rifampicin. Rifampicin has better drug interaction level (50%) when compared with Ethambutol with 70% drug interaction level. Rifampicin (99.5%) has a higher degree of adverse drug reaction than Ethambutol (95%).

Table 5: EFFECTIVENESS RATING FOR ANTITUBERCULOSIS DRUGS

Criteria	Cap. Rifampicin	Value	Tab Ethambutol	Value
1. Spectrum of antituberculous activity **Assumption:**	Bactericidal in action (extra cellular and intracellular activity). Use with other drug to delay or prevent development of Rifampicin resistance Both of them can achieve the desired therapeutic outcome if used effectively; 100% sensitivity assumed	100%	Bacteriostatic within some reported bactericidal activity (intracellular and extracellular) It suppressed the resistant mycobacterium tuberculosis	**100%**
Pharmacokinetics	Oral absorption: 70% Presystemic metabolism: Nil Bioavailability: 70% Plasma t½ 2-5h Frequency of administration o.d	70%	Oral absorption: 80% Presystemic metabolism: Nil Bioavailability: 80% Plasma t½ 10-15h Frequency of administration o.d	**80%**
3. Interaction	Microsomal enzyme inducer 50% Food can effect oral absorption 50%	50%	Non microsomal enzyme inducer Food effect oral microsomal	**70%**
4. Adverse drug reaction (ADR)	Hypertsensitivity fewer than 1 % Facial flush Itching Hepatitis occurs rarely Causes harmless orange-red discolouration of body secretions and other body fluids. Tolerability = 100-1%	99%	Dose dependent optic neuritis (easily reversible) at 15mg: at 15mg/kg/day<1% at 25mg/kg/day <5% Colour blindness Allergic rashes, Jaundice reported Tolerability (100-5%)	95%

Table 6 shows the Decision table using two options I and II to compare cap. Rifampicin and tab Ethambutol with Ethambutol accounting for 89% effectiveness and Rifampicin accounting for 83.8% effectiveness. Tab Ethambutol ₦2, 544.30 was found to be more cost effective than cap Rifampicin ₦8, 918.64 (Table 7).

TABLE 6: DECISION TABLE

	Cap RIFAMPICIN (Option I)			Ethambutol tab (Option II)		
Criterio	Value (%)	Assigned weight	Criterion rating	Value (%)	Assigned weight	Criterion rating
1. Spectrum of antituberculous activity	100	0.4	40.0	100	0.4	40.0
2. Pharmacokinetics	70	0.2	14.0	80	0.2	16.0
3. Interaction	50	0.2	10.0	70	0.2	14.0
4. Tolerability	99	0.2	19.8	95	0.2	19.0
Sum of criteria rating		1.0	83.8		1.0	89

STEPS IN CONDUCTING A DECISION ANALYSIS

1. Criterion value x assigned weight (%) = Criterion rating
2. Sum Criterion Rating for each alternative (Effectiveness measure)

Table 7: CALCULATION OF COSTS

Direct medical costs	Cap Rifampicin (Option I)	Tab Ethambutol (Option II)
1. Acquisition cost of drug	600mg o.dx6/12 (C/DDDxDDT) 50.0x168=N 8,400	**800mg o.dx6/12 (C/DDDxDDT) 12.0x168=2,016**
2. Cost associated with preparation, dispensing and administration of drug	Pharmacist, ₦0.4830 x 80 sec.= ₦38.64	**Pharmacist, N0.4830 x 100sec =N48.30**
3. Travel cost (to patient) assuming N80/Trip	80 x 6 (assuming 6 visits on monthly basis) ₦480	**80 x 6 =N480**
Total	**₦8,918.64**	**₦2,544.3**

Physician office visit assumed to be equal for both option
Indirect cost not included

COST EFFECTIVENESS ANALYSIS (CEA): COST/EFFECTIVENESS

Option I: Rifampicin Cap: cost = N8,918.64, Effectiveness = 83.8;
CEA = 8,918.64 = 106.43/unit of effectiveness
83.8

Option II: Ethambutol tab: Cost = 2,544.3, Effectiveness = 89;
CEA = 2,544.3 = 28.59/unit of Effectiveness.
89

Option II: Ethambutol tab is more cost effective

SENSITIVITY ANALYSIS

i. Increasing the cost of ethambutol tab even by 200% (5,088.6);
CEA = 5,088.6 = 57.18/unit effectiveness
89

ii. Decreasing the effectiveness of ethambutol to 83% (Rifampicin value);= 2,544.30 = 30.36/unit of effectiveness
83.8

iii. Decreasing the cost of Rifampicin by 50% (4459.32);
CEA = 4459.32 = 50.10/unit effectiveness
89

iv. Increasing Pharmacist Dispensing time of ethambutol to 180secs (2582.94);
CEA = 2582.94 = 29.02/unit effectiveness
89

The decision still remain valid justifying the cost effectiveness of ethambutol in patient without eye problems.

DISCUSSION

The total number of antimicrobials drugs prescribed ranged from 3 to 5 with mean of 3.6(Table 1). This is similar to findings conducted in a secondary health care facility in Lagos,Nigeria[12] and health care facility in Ilorin which was 3.99[13].The study indicated that tertiary level in Ilorin northwest had 3.5[14] and at primary healthcare

facility Ilorin north central was 4.5 and at health care facility it was 3.9[15] .

Prescription that had antimicrobials prescribed for females was the highest percentage being 61% and for the male, it was 39.00% (Fig 1). Since pregnant women and children received free medical services, it is difficult to ascertain the high cost attributed to these groups.

The percentage of antimicrobial drugs prescribed was found to be Quinolone 31% followed by penicillin 23.4% and imidazole 17% (Table 2). This result was different from the one obtained in a secondary health care facility in Lagos[12] and tertiary health care facility in Ilorin[17]. The disparity could be attributed to drug supply and stocking systems at the pharmacy in the various institutions. Extensive use of antibiotic is not appropriate. The in appropriate use of antibiotics has been related to addition cost of the drug consequences to the patient and resistance to microbial flora within the hospital[18].

The total costs in Naira for antimicrobials prescribed at the General Hospital, Minna was found to be NGN652,382 an equivalent of 4,263.92 U.S. dollars, with Penicillin being 56,222.00 naira, Cephalosporin 80,160.00 naria, Quinolones 261,840.00 naria, Imidazoles 22,000.00 naira, Tetracycline 173,560 naira Antitubercular and Aminoglycosides and Macronides accounting for 58,600.00 naira (Table 2). This result is different from what was obtained in a secondary health care facility in Lagos [12] and a tertiary health care facility in Ilorin.[17] This difference can be attributed to difference in drug supply and distribution system at the pharmacy department in the various institutions.

At the General hospital, Minna, the cost per defined daily dose (DDD) of branded antimicrobials was found to be more than the generic antimicrobials. (Table 3). This is because the branded antimicrobials are usually more expensive than the generic ones. The generic substitution has long been applied in the formulary system because they are cheaper. The branded substitution however, has the benefit of optimal drug therapy. The generic substitution has the benefit of direct drug inventory cost saving.[19] Most of the patients who visit this hospital are medium to low income class and generic substitutions will be more affordable to these classes of people. UNDP reports that over 70% of Nigerians earn below 1 dollar per day.

In a study conducted by Akande and Alonge at a secondary health care facility in Ilorin, it was reported that irrationally prescribed antibiotics resulted in 26.7% reduction in the cost of drugs per prescription[14], hence the cost effective analysis (CEA) which can be described as an examination of the costs of two or more programmes which have the same clinical outcome as measured in physical units such as lives saved or reduced morbidity should be considered to justify pharmacoeconomics to the patients.

There is however no rationale for branded substitution to be prescribed when the generic equivalent is guaranteed for therapeutic effectiveness.[20]

Generic drug programmes are probably the most relevant economic strategy for drug supply recently.[21] Table 4 indicates that cost minimization analysis (CMA), which can be described as an examination of the costs of two or more programmes which have the same clinical outcome as measured in physical units such as lives saved or reduced morbidity, can be used to improve efficiency and effectiveness. This also helps to improve the awareness of drug cost among clinicians. In general, drugs monotherapies and combination therapies are listed with their defined daily dose (DDD) in some phamacopeas.[16]

Effectiveness rating obtained for Rifampisin and Ethambutol, the antitubercular drugs were 99% and 95% respectively (Table 5). This is similar to a study conducted by Giwa Osagbemi *et al* in a tertiary health care institution in Zaria.[22]

Decision analysis technique which offers a method of pictorial representation of treatment decisions, was conducted by calculating sum of criteria rating for Rifampicin and Ethambutol using two different options I and II. (Table 6). The total direct medical costs for Rifampcin and Ethambutol using two different options I and II are indicated in table 7.

Cost effectiveness analysis showed that Rifampicin has 106.43 per unit of effectiveness using option I and Ethambutol has 28.59 per unit of effectiveness using option 11, thereby justifying Ethambutol as more cost effective drug than Rifampicin in the treatment of antituberculosis. This result is different from what was obtained in a tertiary health care institution in Northern Nigeria for Ethambutol with 8.40 per unit of effectiveness.[22] The difference in results may be due to different locations, time when studies were conducted and incremental cost effect.

CONCLUSION AND RECOMMENDATION

It was observed that some classes of antimicrobials were prescribed more frequently than others; therefore, stocking and cost of antimicrobial therapy to the patient need attention in order to contain cost and development of resistance to antibiotics.

Database that include pharmacoeconomic evaluation results, adverse drug reaction, bioavailability, bioequivalence and absolute bioavailability of various drugs should be looked into and made available to the public either through pharmacovigilance centre or functional Drug Information Centre.

Drugs and therapeutics committee (DTC) in the health institutions should be looked into and reactivated if non-functional.

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