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Original Article

COST EFFECTIVENESS OF SIX DRUGS FOR THE TREATMENT OF *PSUEDOMONAS AERUGINOSA* INFECTIONS IN NIGERIA

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ABSTRACT

Objective: The objective of the study was to determine the most cost effective antibacterial agents in the treatment of *Pseudomonas aeruginosa* infections in Lagos metropolis.

Methods: Cost effectiveness analysis of ciprofloxacin, ceftazidime and gentamicin among routinely used antibacterial agents and amikacin, meropenem and imipenem/cilastatin for resistant isolates identified to be most effective agents against 480 clinical isolates of *Pseudomonas aeruginosa* obtained from the Six hospitals was carried out on the basis of societal perspective using 'decision table" as an analytical model. Criteria considered in the model included degree of efficacy of the agents, adherence tendencies and tolerability. The coefficient of cost effectiveness was determined for each of the drugs and compared.

Results: Ciprofloxacin tablet is dominantly more cost effective than gentamicin and cetazidime injections for sensitive isolates of *Pseudomonas aeruginosa* in Lagos Metropolis with the least cost effectiveness ratio of NGN4241.82 (USD28.28) from societal perspective. Amikacin is the most cost effective among the drugs evaluated for resistant isolates with a cost effectiveness ratio of NGN50,118.85 (USD334.13). Incremental cost analysis showed that additional benefit gained using a more expensive ceftazidime with higher probability of cure over gentamicin will cost NGN157, 340.43 (USD1, 048.94) per treatment success.

Conclusion: Ciprofloxacin tablet should be used in preference to ceftazidime and gentamicin injection if indicated in the treatment of *sensitive Pseudomonas aeruginosa* infections and amikacin for resistant isolates due their cost effectiveness.

Keywords: Pharmacoeconomics, Cost Effectiveness Analysis, Cost of Therapy, Cost of illness, Pseudomonas *aeruginosa,* Antibacterial Therapy, Health Economics, Nigeria .

INTRODUCTION

Implications of antimicrobial resistance on public health are becoming increasingly overwhelming [1, 2]. Antimicrobial drug availability and affordability with assured efficacy can hardly be guaranteed for a good proportion of infections in many developing countries of the world [3]. In most countries of the world including developed ones with economic downturn, coping with skyrocketing cost implications of antimicrobial resistance is a big challenge [2]. Spectre of post antibiotic era is imminent [4] except with drastic proactive measures. The weak institutional and individual patient capacity to manage infections, poor infection control and, weak implementation of antimicrobial policy/surveillance activities in developing countries [5] are of serious concern. Other factors that complicate the picture include poor environmental sanitation, fake drug products, low standard of living, low per capital income/health spending [6] poor governance in the health system [7] and irrational/misuse of antimicrobial agents.

Pseudomonas aeruginosa which is implicated in most health-care-associated infections in Africa [8] is particularly outstripping the infection management capacity of developing countries where most of the available drugs are becoming obsolete resulting from innate and/or acquired resistance. Drugs presently regarded as major antipseudomonas such as amikacin, imipenen and meropenem among others [9] are neither available in most of the health facilities nor affordable to majority of the populace who live below poverty line earning less than US$1.00 per day. More so, commonly available and affordable agents in routine use such as quinolones, cephalosporins, and some aminoglycosides are gradually losing their clinical value with continually reducing antibacterial susceptibility [2, 4, 5, 9]. Published information on cost effectiveness of these agents in developing countries is rare which could be useful in making necessary decisions and policy formulation. This study applies Cost Effectiveness Analysis (CEA) [10, 11] to evaluate six efficacious agents in the treatment of *P. aeruginosa in* Lagos metropolis from a societal perspective. Research similar to this for *P. aeruginosa* has not been reported in Nigeria.

MATERIALS AND METHODS

The study was carried out in Six centres within Lagos Metropolis which include two tertiary hospitals with a monthly turnover of about 10,000 patients each, a specialist hospital, a referral health care centre and two private hospitals. Approval for the study to be conducted was granted by all the hospitals. Four hundred and eighty isolates of *P. aeruginosa* were considered in all out of which 390 clinical isolates were identified in a prospective study conducted between the year 2006 and 2011, using standard techniques [12] and subjected to antibacterial susceptibility testing using disk diffusion method [13,14]. The various antibacterial agents were classified as "resistant", "intermediate sensitive" or "sensitive" based on interpretative chart of Clinical and Laboratory Standard Institute [13, 14] for the various isolates. The three most efficacious antibacterial agents in routine use from the antibacterial susceptibility testing namely ciprofloxacin, ceftazidime and gentamicin were selected for the cost effectiveness analysis (CEA). In addition, information on susceptibility patterns of 90 clinical isolates from recent literature for three relatively newer drugs namely amikacin, meropenem and imipenem [9] which are yet to be in routine use was reviewed as well and included in the CEA. The CEA for the agents was carried out on the basis of societal, perspective using 'decision table" as an analytical model [15, 16]. For the societal perspective, cost relating to drugs, diagnosis/monitoring, personnel, transport and indirect cost (loss in productivity) were considered. For purpose of comparison, costs relating to drugs, diagnosis/monitoring and personnel were considered in the case of health care perspective while costs relating to drugs and diagnostic test were considered in the case of third party perspectives.

Determination of costs

Direct (cost of drugs, diagnosis/monitoring, personnel and transportation) and indirect (loss of productivity) costs were included in cost of therapy evaluation. Antibacterial cost was the average wholesale price (AWP) in Lagos metropolis in addition to handling costs. Defined daily dose was used as recommended for cost analyses of drugs [17, 18] and minimum therapy duration of seven days was assumed for each drug. The used defined daily dose of ciprofloxacin tablet was 1000mg in two divided doses, ceftazidime injection 1000mg three times daily, and gentamicin injection 240mg in three divided doses. The DDD used for amikacin was 1000mg in two divided doses, while 1500mg in three divided doses and 2000mg in four divided doses were used for meropenem and imipenem/cilastatin respectively. The cost for diagnostic (microscopy, culture and sensitivity) applied in the teaching hospital was used. For personnel cost, the human capital method [19, 20] was applied. Average time taken for completion of tasks such as consultation, dispensing and drug administration was determined after 15 random observations of each task by respective personnel. The salaries of health professionals were obtained from the accounts department of the hospitals and the mean salary per minute calculated based on the total inputted hours by the staff at work [21]. Transportation cost was calculated as the average transport cost per return trip to the hospital (NGN200.00 (US$1.33) by the patients.

The indirect cost due to loss in productivity as a result of hospital attendance by the patients was determined using the human capital method as well [19, 20]. This was calculated based on time spent in the hospital and loss in earnings on a 40-hour, 5 day working week. An average family daily loss of five hours of work was assumed and loss in productivity (indirect cost) per hour for the least paid patient who is a government worker which is NGN102.27 (US$0.68) was used. This includes time spent for diagnostic testing, treatment and transportation. A minimum of two visits, the usual practice in the hospital was assumed, the first for consultation and the second visit after microscopy, culture and sensitivity test has been carried out. Additional two hours' work loss was assumed per day for daily injection. There was neither discounting of cost nor adjustment for inflation as all the costs occur within one year of analysis.

Effectiveness rating

In the analytical model, the criteria considered in the e*ffectiveness rating* were degree of efficacy, adherence tendency and humanistic outcomes[16]. The values of the degree of efficacy; a proxy measurement of cure rates for ciprofloxacin, gentamicin and ceftazidime were obtained from the results of antibacterial susceptibility testing of 390 isolates of *P.aeruginosa* for "sensitive" isolates of Clinical and Laboratory Standard Institute [13,14]. Efficacy ratings for amikacin, meropenem and imipenem were obtained from literature in which Ninety isolates of *P.aeruginosa* from South Western Nigeria [9] were evaluated. Intermediately sensitive and resistant clinical isolates were excluded. Appropriate literature was also reviewed for incidences (rate) of adverse drug reactions for these antibacterial agents [22-26]. Humanistic outcome was measured as tolerability prorated from literature reported degree of adverse drug reactions events, risk of infection and pains from drug administration. For each of the criterion in the rating, weight was then assigned based on consensus amongst the authors. The degree of efficacy, adherence tendency, and tolerability were assigned weights of 0.5, 0.2 and 0.3, respectively [16]. The frequency of dosing with once daily administration was allotted 100% adherence tendency while twice daily, three times daily and four times daily administration were allotted 50.0%, 33.3% and 25.0% adherence tendency respectively [16,27]. The degree of effectiveness of each antibacterial agent was the sum total of the criterion rating which was calculated as the product of criterion value and assigned weight [15]. The coefficient of CEA-cost effectiveness ratio was then determined by dividing the total cost of therapy by degree of effectiveness obtained from decision analysis. Sensitivity analysis was carried out by varying the effectiveness rating (the sum of criterion rating of efficacy degree, adherence tendency, and tolerability) until effectiveness index or cost calculated did not vary significantly between the various options.

Incremental or Marginal Cost Analysis

Incremental Cost Analysis (Incremental effectiveness ratio-ICER) which assesses the additional cost that one treatment impose over another compared with the benefits or successes it provides[28] considering societal perspective for ceftazidime injection was carried out to know the additional benefit gained using a more expensive ceftazidime with higher probability of cure over gentamicin injection which has lower cost- effectiveness ratio. Incremental cost effectiveness ratio (ICER) was also determined for the use of amikacin, meropenem and imipenem/cilastatin over the older drugs in routine use.

Incremental cost effectiveness ratio= Cost of Ceftazidime - Cost of Gentamicin÷Effectiveness probability of Ceftazidime – Effectiveness probability of Gentamicin

RESULTS

Cost of Therapy

From the societal perspective, the cost of therapy per patient was highest for ceftazidime injection at NGN30, 985.59 (USD206.57) followed by gentamicin injection and ciprofloxacin tablet at NGN8800.59 (USD58.67) and NGN3291.65 (USD21.94) respectively for routine antibacterial agents. The antibacterial cost of ceftazidime injection of NGN24, 675.00(USD164.50) was higher than those of either ciprofloxacin tablet (NGN600.00) (USD4.00) or gentamicin injection NGN490.00 (USD3.27). Also, the personnel, transportation and indirect costs incurred using ceftazidime and gentamicin injection were higher than that ciprofloxacin tablets (Table 1). The proportion of antibacterial cost constituted 18.2%, 79.6% and 5.6% of societal cost of therapy for ciprofloxacin, ceftazidime gentamicin respectively. Higher therapy costs were obtained for the relatively newer agents meant for resistant isolates. The highest value of NGN90, 310.40 (USD602.07) was obtained for imipenem/cilastatin followed by meropenem [NGN46, 945.40(USD312.97)] while amikacin was the least [NGN43603.40 (USD290.69)]. The cost of therapy was much lowered for hospital/health care and third party payer perspectives than societal perspective (See Table 2 for details).

Effectiveness Rating

Among the routinely used antibacterial agents, the degree of efficacy was highest for ciprofloxacin followed by ceftazidime. The least adherence tendency value was obtained for ceftazidime and gentamicn. Similarly, ciprofloxacin tablet gives the highest value of tolerability. The overall criterion rating values for effectiveness of ciprofloxacin tablet, ceftazidime injection and gentamicin injection were 77.6% (0.776), 70.4% (0.704) and 56.3% (0.560) respectively. For newer agents the overall effectiveness rating were as follows; amikacin 87.0% (0.870), meropenem 83.6% (0.836) and imipenem/cilastatin 83.6% (0.836). (See Table 3 for details)

Cost Effectiveness Analysis

Ciprofloxacin tablet with effectiveness rating of 0.776 has a cost effectiveness ratio (CER) (coefficient of Cost Effectiveness Analysis) of NGN4241.82 (US$28.28), NGN2408 (US$16.05) and NGN2061.86 (US$13.75) for societal, health care and third party payer perspectives respectively and is dominantly cost effective.

The Coefficient of CEA obtained for ceftazidime injection with effectiveness rating of 0.704 was NGN44013.62 (US$293.42) for societal perspective while NGN37131.51 (US$ 247.54) and 36470.17

(US$243.13) were obtained for health care and third party payer perspectives. For gentamicin injection, the various coefficient values were NGN15631.60 (US$104.21), NGN7025.91 (US$46.84) and NGN6198.93 (US$41.33) for societal, health care and third party payer perspectives respectively. For newer agents meant for resistant isolates, amikacin is the most cost effective with a cost effectiveness ratio of NGN50,118.85 (USD334.13) followed be meropenem with CER of NGN56,154.78 (USD374.37) and imipenem/cilastatin the least cost effective with CER of NGN108026.79 (USD720.18). (Table 4)

The results remain valid with sensitivity analysis. When the effectiveness index of gentamicin was increased to 0.776 the value for the most cost effective option, the cost effectiveness ratios obtained for the societal, health care and third party payer perspective were NGN11340.00 (USD75.6), NGN5097.41(USD33.98) and NGN4497.42(USD29.98) respectively, which were many folds higher than those obtained for ciprofloxacin tablet. Increasing the therapy cost of ciprofloxacin tablet in excess of 100.0% did not affect the result with respective CER of NGN8481.95 (USD56.55), NGN4816.11 (USD32.11) 4123.71 (USD27.49)for societal, health care and third party payer perspectives. Among the drugs for resistant isolates, amikacin being dominantly cost effective still remain the most cost effective with sensitivity analysis of the variables (therapy cost and effectiveness).

Table 1: Cost of Therapy per Patient in the Treatment of *P aeruginosa Infections*

S/N	Cost Component	Cost Antibacterial Treatment Options		
		Ciprofloxacin Tablet 1000mg (500mg every 12 hour) NGN (US$)	**Ceftazidime injection 3000mg (1000mg every 8 hour) NGN (US$)**	**Gentamicin injection 240mg (80mg every eight hour) NGN (US$)**
1	Antibacterial Cost	600.00(4.00)	24,675.00(164.50)	490.00(3.27)
2a	Diagnostic Test	1000.00(6.67)	1000.00(6.67)	1000.00(6.67)
2b	Cost Renal function Test	0.00(0.00)	0.00(0.00)	2000.00(13.33)
3	Personnel Cost	268.65(1.77)	465.59 (3.10)	465.59(3.10)
4	Transport Cost	400.00(2.67)	2800.00(18.67)	2800.00(18.67)
5	Indirect Cost	1023.00(6.82)	2045.40(13.64)	2045.40(13.64)
	Cost of Therapy	**3291.65(21.94)**	**30985.59 (206.57)**	**8800.59(58.67)**

Exchange rate used: NGN150.00=US$1.00

Table 2: Cost of Therapy per Patient for various perspectives in the Treatment of *P aeruginosa* Infections

S/N	Perspective /Cost Component	Cost of Antibacterial Treatment Options		
		Ciprofloxacin Tablet 1000mg (500mg every 12 hour) NGN (US$)	**Ceftazidime injection 3000mg (1000mg every 8 hour) NGN (US$)**	**Gentamicin injection240mg (80mg every eight hour) NGN (US$)**
1	Societal Perspective (Drugs, Diagnostic/Monitoring, Personnel, Transport and Indirect Costs)	3291.65(21.94)	30985.59 (206.57)	8800.59(58.67)
2	Health Care Perspective (Drugs, Diagnostic/Monitoring, Personnel)	1868.65(12.46)	26140.59(174.27)	3955.59(26.37)
3	Third Party Payer Perspective (Drugs, Diagnostic/Monitoring Costs)	1600.00(10.67)	25675.00 (171.17)	3490.00(23.67)

Exchange rate used: NGN150.00=US$1.00

Table 3: Decision Analysis Table of Drugs for Treatment of *P. aeruginosa* Infections

S/N	CRITERIA	OPTION I Ciprofloxacin Tab			OPTION II Ceftazidime injection			OPTION III Gentamicin Inj		
		Value (%) (a)	**Assigned Weight (b)**	**Criterion Rating (a*b)**	**Value (%) (a)**	**Assigned Weight (b)**	**Criterion Rating (a*b)**	**Value (%) (a)**	**Assigned Weight (b)**	**Criterion Rating (a*b)**
1	Degree of Efficacy	78.9*	**0.5**	39.5	75.0*	**0.5**	37.5	56.0*	**0.5**	28.1
2	Adherence Tendency	50.0[16]	**0.2**	10.0	33.3[16]	**0.2**	6.7	33.3[16]	**0.2**	6.7
3a	Humanistic Outcome (Local effect/Tolerability)	100.0	**0.1**	10.0	80.0	**0.1**	8.0	40.0	**0.1**	4.0
3b	Humanistic Outcome (ADR rating/Tolerability)	95.5[22]	**0.2**	18.1	91.0[23,24]	**0.2**	18.2	87.5[25]	**0.2**	17.5
	Sum of criteria rating (Effectiveness measures)	NA	**1.0**	77.6	NA	**1.0**	70.4	NA	**1.0**	56.3

References: Cano and Fujital 1988[15], Effectiveness Rating of Drugs for the treatment of *P. aeruginosa* Infections (Appendix I; Table 5), * Obtained from the degree of antibacterial susceptibility testing for highly sensitive strains, Suleiman et al 2012 [16]; Mandell, 2003 [22]; AHFS, 1999[23]; Bank and Kammer 1983 [24]; Kahmeter and Dahlager, 1984 [25].

Table 4: Decision Analysis and Cost Effectiveness Ratio of Drugs for Treatment of *Resistant P. aeruginosa* Infections

Drugs/Criteria	Assigned weight (a)	Amikacin inj (500mg 12 hourly)		Meropenem inj (500mg 8 hourly)		Imipenem/Cilastatin inj (500mg 6 hourly)	
		Value (%)(b)	Criterion rating (a*b)	Value (%) (b)	Criterion rating (a*b)	Value (%)(b)	Criterion rating (a*b)
Degree of efficacy[9]	0.5	100.0	50	100	50.0	100	50.0
Adherence.Tendency[16]	0.2	50.0	10	33.0	6.6	33.0	6.6
Tolerability[16,26]	0.3	90.0	27	90..0	27.0	90.0	27.0
Effectiveness Measure(c)	1.0 (100.0)	-	0.870 (87.0)	-	0.836 (83.6)	-	0.836(83.6)
Cost of Drug for 7 days (d)		NGN35,490.00 (USD236.60)		NGN40,635.00 (USD270.90)		NGN84,000.00 (USD560.00)	
Cost of Therapy (societal) for 7 days (e)		NGN43603.40 (USD290.69)		NGN46945.40(USD312.97)		NGN90310.40 (USD602.07)	
Cost Effectiveness Ratio (e/c)		*NGN50118.85 (USD334.13)*		*56154.78 (USD374.37)*		*108026.79 (USD720.18)*	
ICER over ciprofloxacin tab		NGN428,848.40 (USD2858.99)		NGN727,562.50 (USD4850.42)		NGN1,450,312.50 (USD9668.75)	
ICER over ceftaxidime inj		NGN76,010.00 (USD506.74)		NGN120,907.65 (USD806.05)		NGN449,430.38 (USD2996.20)	
ICER over gentamicin inj		NGN113,364.20 (USD755.76)		NGN139,724.58 (USD931.50)		NGN298,570.7 3 (USD1990.47)	

Susceptibility -100.0% (Okesola and Oni, 2012 [9]) Adherence Tendency (Suleiman et al 2012 [16]) Adverse Drug Reactions- Amikacin 1%-10% (average= 5.5%), Imipenem /Cilastatin 1%-10% Meropenem 1-10% (Lacy et al 2011 [26]) ICER= Incremental Cost Effectiveness Ratio [28].

Incremental Cost-Effectiveness Ratio: Incremental cost analysis showed that additional benefit gained using a more expensive ceftazidime but with higher probability of cure over gentamicin with lower cost- effectiveness ratio will cost NGN157,340.43 (USD1048.94) per treatment success.

Incremental cost effectiveness ratio by using amikacin over ciprofloxacin tab, ceftaxidime inj and gentamicin inj will also cost NGN428, 848.40 (USD2858.99), NGN76,010.00 (USD506.74), NGN113,364.20 (USD755.76) per treatment success respectively (See Table 4 for details).

Appendix I (Table 5): Effectiveness Rating of Traditional Drugs for the Treatment of *P aeruginosa* Infections

S/N	Criteria	Option I		Option II		Option III	
		Ciprofloxacin Tab Criteria Description	Value (%)	**Ceftazidime inj** Criteria Description	Value (%)	**Gentamicin Inj** Criteria Description	Value (%)
1.	Efficacy	Degree of Efficacy	78.9*	Degree of Efficacy	75.0*	Degree of Efficacy	56.0*
2.	Adherence Tendency	Administration frequency (Twice daily)	50.0[16]	Administration frequency (Three times daily)	33.3[16]	Administration frequency (three times daily)	33.3[16]
3a.	Humanistic Outcome	Local effect; pain at administration site, risk of infection (0.0%) Tolerability (100-0)	100.0	Local effect; pain at administration site, risk of infection; phlebitis(2%-20% [21]) Tolerability (100.0-20.0)	80.0	Local effect; pain at administration site (100.0%), risk of infection, phlebitis (20.0%) [25] Tolerability (100-60)	40.0
3b.	Humanistic Outcome	Adverse drug reactions (ADR); occurs 5.0-14.0% of patients (Average=9.5%) [22] Nausea 5.2%, Abdominal cramp 1.7%, Diarrhoea 2.3%, Rash 1.1% Tolerability (100-9.5)	90.5%	Adverse drug reactions (ADR) 10.0% of patients Haematological 7.0% Diarrhoea 2.0% [23,24] Tolerability (100-9.0%)	91.0	Adverse drug reactions [25] Ototoxicity; 1.0%-5.0% of patients- often irreversible, Nephrotoxicity; 10%-15% -reversible (average=12.5%) Tolerability (100-12.5%)	87.5

References: Cano and Fujital 1988 [15]; Effectiveness Rating of Drugs for the treatment of *P. aeruginosa* Infections obtained from the degree of antibacterial susceptibility testing for highly sensitive strains*, Suleiman et al 2012 [16]; Mandell, 2003[22]; AHFS, 1999 [23]; Bank and Kammer 1983 [24]; Kahmeter and Dahlager, 1984 [25].

DISCUSSION

This study has revealed that ciprofloxacin tablet is the most cost-effective treatment for sensitive isolates of *P. aeruginosa* in Lagos metropolis, when compared with ceftazidime and gentamicin injections among other drugs in routine use based on its lowest cost effectiveness ratio while amikacin injection is also dominantly more cost effective for resistant isolates relative to meropenem and imipenem/cilastatin injections.

The major strength of this study is the use of relatively current efficacy data from the study locality as the literature reported efficacy value often drops over time partly because of the development of acquired resistance. Other strengths are the inclusion of various cost components including indirect cost and the comparison with other perspectives which can increase the applicability of the results. The robustness of the analysis is strengthened by the computation of incremental cost effectiveness ratio in addition to sensitivity analysis which did not change even with many folds increment in cost or effectiveness in favour of less cost effective options. Major limitations of this study are the reliance on susceptibility data as a proxy cure rate, the difficult accuracy in the allocation of assigned weights to the various outcomes. In real setting a consensus between the researcher and policy makers would minimise this type of challenge. Relevant sensitivity analysis can also be carried out with various assigned weights and the differences compared. The fact that allocation of assigned weight to each criterion, a consensus among authors was predetermined at the planning stage and more importantly all the options were treated in the same way limits the subjectivity. Regardless of who decide the allocation of assigned weight, efficacy is the most important criterion in antibacterial therapy. Other limitation include the relatively small number of isolates, reliance on in-vitro evidence and lack of differentiation between extended spectrum beta lactamase *P. aeruginoasa* producers and non producers. However, some of the isolates used for the newer agents were extended spectrum beta lactamase producers. Reports from the data for drugs for resistant isolates indicated 22.2% of the *P. aeruginoasa* isolates to be extended spectrum beta lactamase producers [9] yet the three antibacterial agents had 100.0% susceptibility results.

Ciprofloxacin, the most cost effective agent in this study is a broad spectrum antibacterial agent that can be misused and therefore needs regular drug utilisation review which is also at a cost. Another drawback of ciprofloxacin is that it is not recommended for children and discouraged in adolescents as a result of its tendency for arthropathy hence safety consideration is vital when considering its use. In very serious and life threatening *Pseudomonas* infections such as endocarditis, pneumonia,, bacteraemia, urinary tract combination of an aminoglycoside with antipseudomonas penicillin or cephalosporin are recommended [29-32]. For some disease conditions such as meningitis, ceftazidime is much better due to higher penetration and bioavailability in subarachnoid space. For ophthalmic use, gentamicin or ciprofloxacin eye drops would be preferred. For pseudomonas infections in cystic fibrosis, aerosolised aminoglycoside or ceftazidime may also be employed.

The benefits of using the more clinically efficacious but more expensive ceftazidime over gentamicin was obvious in the additional benefits gained (incremental cost effectiveness) per treatment success of its preferential uses if indicated for patients that can afford it. The use of the most efficacious agents reduces antibacterial resistance episodes as well; however misuse may eventually affect its life span. Resistant strain of *Pseudomonas aeruginosa* to ciprofloxacin among other drugs has been widely reported [5, 9, 32, 33]. Monitoring or preventing resistance to drugs by microbes is also at a cost but much lesser than the cost implications of antibacterial resistance to the society [34].

As obvious in the exorbitant therapy cost of drugs for resistant isolates, these agents are unaffordable to majority of individual patients with poor per capita income and most of whom are not in any form of health insurance coverage. Routine use of such high cost drug options could deplete any health care system regardless of premium pool of funds as well and is equally unrealistic with poorly capitalised health insurance scheme in most developing countries.

Therefore, efforts must be made to optimise the routinely available drug options particularly in developing countries where antibacterial resistance database and surveillance are very poor and per capita health spending is also very low. The difference in therapy cost for *Pseudomonas* isolates that were sensitive to ciprofloxacin and gentamicin as compared to the cost of amikacin and others for resistant isolates indicates what the cost implications and economic burden of multidrug resistant infection could be on the patients and health care system. A mean cost of hospitalization for multidrug resistant *P. aeruginosa* of USD54,081.00 compared to a mean cost of US$22,116.00 hospitalization for patients with susceptible *P. aeruginosa* was previously reported [35].

Appropriate combination therapy of routinely available agents as outlined for serious infections above should be evaluated as this may be more cost effective than newer agents if indicated. However, the relatively newer agents need to be made available for resistant isolates as reserved options.

The use of ciprofloxacin infusion instead of the tablet (which is the most cost effective option) would have to be employed among some In-Patients which would be at higher cost to the various perspectives. In such situation timely switch to oral therapy is very important and would save a lot of costs directly and indirectly. One sequential therapy of quinolones infusion followed by oral forms resulted in a 53% decrease in intravenous quinolones and increment of oral forms by 35.0% and achieved a global savings of US$41,420.00 (NGN5,374,600.00) for the hospital for these drugs during the period under consideration [36].

Suggested modalities to curtail antibacterial resistance and its economic impact include development of new drugs, surveillance, implementing infection control measures, adapting new technology for detecting new mode of antibacterial resistance, educational programmes, optimising antibacterial agents' utilization and influencing drug selection [34].

Recommendation for further research include periodic identification of extended spectrum beta lactamase among *P. aeruginosa* isolates in Lagos metropolis to establish their antimicrobial resistance profiles and cost effective treatment patterns as well as determination of actual cure rates among treated patients as clinical outcome.

CONCLUSION

Ciprofloxacin tablet should be used in preference to ceftazidime and gentamicin injection in the treatment of sensitive *P. aeruginosa* infections in Lagos metropolis due to of its better cost effectiveness. For resistant isolates amikacin is the most cost effective among evaluated options. Additional benefit gained using a more expensive ceftazidime but with higher probability of cure over gentamicin with lower cost- effectiveness ratio will cost NGN157,340.43 (USD1,048.94) per treatment success and minimises the development of antibacterial resistance.

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CONFLICT OF INTEREST

There is no conflict of interest associated with this study.

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