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Poor compliance to antibiotics dispensed in a tertiary care hospital: A follow up study from Sri Lanka.

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Abstract

Introduction: Poor compliance with antibiotics is a well described phenomenon. This has contributed to the increased burden of antibiotic resistance in many countries.

Objectives: This study was conducted to investigate patient compliance with antibiotic regimens in Sri Lanka.

Methods: Patients who received antibiotics from one outlet of the outdoor pharmacy in Teaching Hospital, Karapitiya were enrolled into the study. An interviewer administered questionnaire was used to collect initial data. Three days after dispensing, follow up telephone calls were made to obtain information about adherence to dose and dose frequency.

Results: Out of total 509 patients participated for the initial data collection, 318 (62.4%) responded to the telephone interview. Among the respondents, 169 (53.1%) were compliant with the antibiotic regimen. Of them 143 (45%) and 26 (8.1%) were fully compliant and marginally compliant with the antibiotic regimens respectively. The total number of patients who did not strictly adhere to the dose and frequency instruction were 28 (8.8%) and 171 (53.8%) respectively. Commonest reasons for noncompliance were forgetfulness, followed by intentionally withdrawal. Compliance was significantly associated with dosing frequency (X^2=14.1; P=0.007) and indication for commencing antibiotics (X^2=14.2; P=0.014). Postsurgical treatment and urinary tract infection had higher compliance than respiratory tract infections and skin infections.

Conclusions: This study revealed alarmingly high rates of non-adherence to prescribed antibiotic regimens. This can contribute to emergence of resistance to commonly used antibiotics in Sri Lanka.

Keywords: Compliance, antibiotics, infection, pneumonia, resistance

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INTRODUCTION

Antibiotics are considered as one of the most commonly used and therefore one of the highest selling drug classes all over the world. This is more evident in low-income countries where its consumption increased recently [1]. Poor compliance with antibiotic treatment is a well described phenomenon and many reasons have been identified for being non-compliant with the prescribed regimen [6]. Non-compliance can occur when patients miss a dose, stop the drug earlier than expected, take the drug at the wrong time, initiate the treatment later than expected, take multiple does together, take 8-hourly dose as three times a day, take drug holidays etc. The most frequent form of non-compliance is omitting doses and premature halting of antibiotics [2].

Commonly identified reasons for poor antibiotic compliance includes adverse effects of antibiotics, low income of patients, high prices of antibiotics, poor understanding about use of antibiotics, early symptomatic relief, factors related to form or preparation such as unpleasant flavor, difficulties in adjusting the dosing regimen to a patient's lifestyle and poor prescriber's instructions[2-5]. Poor compliance with antibiotics leads to therapeutic failure and re-infection, which leads to additional treatment to the patient and leads to increase the direct and indirect treatment cost of treatment [2]. In addition to that, improper use of antibiotics leads to antibiotic resistance which is a current global health problem.

In some countries, especially in the developing world, antibiotics are freely prescribed and consumed, as a result of which, high rates of antibiotic resistance has been reported [7]. Since the problem is worsening steadily, it has been emphasized that an urgent attention is needed to this global problem to ensure safe use of antibiotics [8]. A comparative study on antibiotic compliance among different countries showed that the compliance is low in low-income countries [9]. Published studies on compliance with antibiotic use in Sri Lanka are sparse, however, it has been observed that there are many irrational practices in the country [10, 11]. We conducted this study to investigate patient compliance with antibiotic regimens dispensed by an outdoor pharmacy of a government hospital in Sri Lanka.

MATERIALS AND METHODS

Patients who received antibiotics from one outlet of the outdoor pharmacy in Teaching Hospital, Karapitiya were enrolled to the study. It was a convenient sample and data was collected in March 2018. An interviewer administered questionnaire (Face validation was done and pretested before use in this study) was used to collect initial data which included duration, frequency and dose of prescribed antibiotics. Demographic data and disease condition as described by patients were recorded. Telephone number of the patient or guardian was requested and patients were informed that they will be contacted for a follow up on antibiotic use. Antibiotic drug among other drugs were introduced to the patient and indicated by a mark in the drug packet. Only those who provided telephone numbers at the initial introduction were included in the study. Patients who were already on antibiotics and those who have hearing impairments were excluded.

Three days after dispensing, follow up telephone calls were made to obtain information from the patients. Details about antibiotic use – adherence to dose and dose frequency were collected. If there was a deviation from the instruction, reasons for that were inquired and noted.

Patients were considered as fully compliant to the drug regimen if they were compliant with the dose, dose frequency and duration of the antibiotic. Instances in which missed single dose or 8 hourly doses taken with little adjustment were considered as marginal compliance. These two groups were collectively named as the "good compliant group" in data analysis. Patients were categorized as "noncompliant" when they had missed more than one dose, not adhering to expected dose frequency and/or not continuing antibiotics to the third day.

At least three attempts were made to contact the patients over the phone on three occasions of a day. If patients were not contactable after

reasonable attempts, the reason for inability to contact was recorded as invalid/wrong phone number, phone not responding, somebody else is responding, and informant being too busy.

Ethical clearance was taken from the Ethic committee of Faculty of Medicine, University of Ruhuna (Ethics Certificate No: 14.12.2017:3.6.3). For analysis, descriptive statistic and Chi-squared test for comparisons were done using SPSS software.

RESULTS

A total of 509 patients participated for the initial data collection and 318 patients (62.4%) responded to the follow up telephone interview. Data were collected from guardian in paediatric patients.

Subsequent analysis on compliance was done using data from 318 participants (patients or guardian in paediatric patients). Age range of patients was 6 months to 79 years (Mean 43± SD 20 years). This includes 278 (87%) adults and 40 (13%) children below age of 16 years. Education level of respondent varied from no schooling 17 (5.3%), primary school 49 (15.4%), ordinary level 146 (46.9%), advanced level 90 (28.3%) and higher education 12 (3.8%).

Among the respondents,169 (53.1%) were noted to have good compliance with the drug regimen. Of them, 143 (45%) were fully compliant with the drug regimen whereas marginal compliance was observed in 26 (8.1%). Noncompliance was observed in the remaining 149(46.9%).

From those respondents (318), 28 (8.8%) and 171 (53.8%) did not strictly adhere to the "dosing" and "frequency" instructions respectively (included marginal compliance patients too). Four patients (1.2%) had both incorrect dose and frequency. All of them who used the correct doses and the correct frequency (the group with compliance) have continued the drug up to the third day, where we interviewed them. Since we interviewed three days after dispensing the antibiotic, we were unable to get an accurate date of termination of antibiotics from most of the non-compliance groups.

Reason for noncompliance was identified in 174 respondents during the telephone interview, where the commonest was forgetfulness (Table 1). Co-amoxiclav was the most prescribed antibiotic 162 (31.8%). Among respondents to follow-up interview, common antibiotic used are Co-amoxiclav 102 (328%), amoxicillin 79 (24%), Cloxacillin 44 (19%), ciprofloxacin 36 (11%), cephalexin 34 (10%) and erythromycin 34 (10%)
There was no relationship between the prescribed antibiotic and compliance. Due to close association and higher usage of amoxicillin and co-amoxiclav, compliance of these two antibiotics was compared. Coamoxiclav had higher compliance (59.8%) compared to amoxicillin (46.8%) thought it is not statistically significant.

Table 1 Reason for the noncompliance

Reason for the non-compliance	Frequency
Forgetfulness	53 (30.9%)
Intentionally not taken	29 (16.6%)
Side effects	23 (13.1%)
School, job, other work	20 (11.4%)
Family commitments	20 (11.4%)
Poor understanding of instruction	11 (6.3%)
Feeling of cure	9 (5.1)
Started treatment from other places	9 (5.1)

Antibiotics were prescribed as three times, two times (bd), three times (tds), four times (qid) per day, 8 hourly and 6 hourly (Table 2). There was a significant association between prescribed frequency and compliance to the regimen (X^2=14.06; P=0.007). According to the results, higher compliance was observed in the patients who were on bd and 8 hourly regimens compared to others.

Table 2 Association between Prescribed frequency and Compliance to the regimen

Frequency	Compliance	Non-compliance	Total
Thrice-a-day (tds)	97(51.1%)	93(48.9%)	190
Twice-a-day (bd)	37(66.1%)	19(33.9%)	56
Six-hourly	12(31.6%)	26(68.4%)	38
Eight-hourly	19(67.9%)	9(32.1%)	28
Four times-a-day (qid)	2(33.3%)	4(66.6%)	6

According to the disease condition provided by the patients, indication for antibiotics was categorized. Few common indication categories were identified and compliance of the patients for each indication category was analyzed (Table 3). Significant relationship between indication and compliance with the regimen was observed (X^2=14.2; P=0.014). Indications such as postsurgical treatment and urinary tract infection have higher compliance than respiratory infections and skin conditions.

Table 3 Association between indication and compliance to the regimen

Indication	Compliance	Non-compliance	Total number
Respiratory conditions	76 (52.8%)	68 (47.2%)	144
Skin conditions	33 (45.20%)	40 (54.8%)	73
Postsurgical treatment	23 (79.3%)	6 (20.7%)	29
Ear Infection	7 (38.9%)	11 (61.1%)	18
Urinary tract infections	8 (80.0%)	2 (20.0%)	10

Further analysis revealed that the compliance was not associated with neither the age of patients (X^2=1.38; P=0.240) or education level of patient or guardian (X^2=14.97; P=0.133). Common reasons for not responding to the telephone interview were invalid or wrong phone number / phone not responding (52.3%), an unrelated person answering the phone (35.7%) and informant being too busy (12%).

DISCUSSION

Despite implementing many antibiotic stewardship strategies, misuse of antibiotics, noncompliance to treatment regimens and emergence of bacterial resistance continue to be global concerns. Providing more evidence to this, this study found that 46.9% of responded patients showed noncompliance to dispensed antibiotics in Sri Lankan setting. If we also considered those with marginal errors, 55% of patients did not show complete adherence to prescribed antibiotic regimen. This was an alarming high rate considering health and economic consequences specially in a tertiary care setting. Poor compliance highlighted in this study also needs to be considered when interpreting clinical response of antibiotics.

Poor compliance with antibiotic regimens has been identified as a major cause of treatment failure [2]. In addition, poor compliance may lead to left-over

antibiotics at home and increase the likelihood of self-medication with the next infection or illness using them. In a study conducted among nine countries, Pechere, *et al* showed that a considerable number of patients deliberately reserve antibiotics for future use specially in developing counties [9].

According to the current study, non-adherence to dose frequency was the main type of noncompliance. From all respondents, 53.8% of patients did not use the correct dose frequency that included missing one or more doses, took less or more frequently than prescribed, or other alterations of frequency. Previous studies also described that alteration of dose frequency was the commonest occurrence among many non-compliance behaviors [2, 12]. Alteration of antibiotic dose was rare and we found only 8.8% of respondents in the current study.

According to the results, forgetfulness was mentioned as the main reason for poor compliance. This was shown as a main reason for poor compliance in previous studies as well [13, 14]. Probably less interest in the antibiotics can be one underlining cause for forgetfulness. Intentional avoidance was the second main reason according to current study and that provides additional evidence for the lack of interest to use the dispensed antibiotics. King, *et al* in their qualitative study described this lack of interest as poor 'effort' or "laziness" and found as the main reason for poor compliance [15]. Considerable number of patients in the current study mentioned family commitment and other commitments such as occupation, school, and other work as reasons for poor compliance. Therefore some social and economic factors which were described in earlier studies [16] would have contributed to poor compliance in this study sample as well. As described in literature very often "feeling better" after a few doses of antibiotics was a reason to stop antibiotics in our sample as well [9] [15] [16] [17].

This result provides evidence that dose frequency of antibiotic influenced the compliance. It is clear that more frequent dosing reduces the compliance. This occurrence was described by previous studies very well and efforts have been taken to reduce the frequency of drug regimen to overcome this problem [12] [18]. 'Started treatment from other places' was found as a reason for noncompliance in the current study. However, that was not well described in previous studies. It is a common practice in Sri Lanka that patients who start treatment from one practitioner, later go to another for second opinion, sometimes within the same day.

Another interesting finding of the study was that compliance depends on the disease condition of the patient. Antibiotic use after surgery and for urinary tract infection (UTI) had higher compliance compared to conditions such as respiratory tract infections. It shows that a patient's interest in using antibiotics depends on the patient's perception of the requirement. This was described in literature; if a patient feels a disease as a severe disease he tends to adhere to the regimen more [2]. After surgery or with conditions like a UTI, the patient is relatively ill and he can easily understand the requirement of antibiotics compared to conditions like respiratory tract infections. Literature reports lower adherence rates (3–60%) for antibiotics prescribed for respiratory tract infections [19-22]. We need to consider the fact that in developing countries such as Sri Lanka, antibiotics are used very commonly for viral respiratory tract infections, which had been shown previously in the same hospital where this study was conducted [23] [24]. Considering this fact, we can assume that patients may in a dilemma about the real requirement of antibiotics for respiratory tract conditions.

This study did not find a relationship between age of the patient, or education level of patient or guardian with antibiotic compliance. It is interesting to see that the education of patient or guardian does not influence the compliance. This is in agreement with previous studies in China,[14] [16], UK [25] and Canada [26]. Probably, the influence of education is masked by other factors such as disease condition and dose frequency. However, in general poor understanding about antibiotics, despite the education level of patients, is well described in a meta analyses done by Gualano *et al* [17].

As a limitation of the study, response to telephone interviews was 62.4% of total participants in initial data collection. In this type of telephone based interviews, response rate is expected to be low [27, 28]. However, when we consider reasons for inability to contact, two main reasons were invalid or wrong phone number, phone not responding and unable to be contacted through given phone number among 88% of non-respondents. These are not patient controlled reasons. Therefore, we do not think that non-responders have any particular pattern, hence we believe that it did not influence the main results of the study.

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Competing interests
There are no conflicts of interest.

REFERENCES

1. Jackson C, Hsia Y, Bielicki JA, Ellis S, Stephens P, Wong ICK, et al. Estimating global trends in total and childhood antibiotic consumption, 2011-2015. BMJ global health. 2019;4(1):e001241. doi: 10.1136/bmjgh-2018-001241. PubMed PMID: 30899565; PubMed Central PMCID: PMC6407570.
2. Kardas P. Patient compliance with antibiotic treatment for respiratory tract infections. The Journal of antimicrobial chemotherapy. 2002;49(6):897-903. doi: 10.1093/jac/dkf046. PubMed PMID: 12039881.
3. Yamamoto Y, Kadota J, Watanabe A, Yamanaka N, Tateda K, Mikamo H, et al. Compliance with oral antibiotic regimens and associated factors in Japan: compliance survey of multiple oral antibiotics (COSMOS). Scandinavian journal of infectious diseases. 2012;44(2):93-9. doi: 10.3109/00365548.2011.619998. PubMed PMID: 22017766.
4. Nightingale R, Colbourn T, Mukanga D, Mankhambo L, Lufesi N, McCollum ED, et al. Non-adherence to community oral-antibiotic treatment in children with fast-breathing pneumonia in Malawi- secondary analysis of a prospective cohort study. Pneumonia. 2016;8:21. doi: 10.1186/s41479-016-0024-8. PubMed PMID: 28702300; PubMed Central PMCID: PMC5471995.
5. Favre O, Delacretaz E, Badan M, Glauser M, Waeber B. Relationship between the prescriber's instructions and compliance with antibiotherapy in outpatients treated for an acute infectious disease. Journal of clinical pharmacology. 1997;37(3):175-8. PubMed PMID: 9089418.
6. Hugtenburg JG, Timmers L, Elders PJ, Vervloet M, van Dijk L. Definitions, variants, and causes of nonadherence with medication: a challenge for tailored interventions. Patient preference and adherence. 2013;7:675-82. doi: 10.2147/PPA.S29549. PubMed PMID: 23874088; PubMed Central PMCID: PMC3711878.
7. Ayukekbong JA, Ntemgwa M, Atabe AN. The threat of antimicrobial resistance in developing countries: causes and control strategies. Antimicrobial resistance and infection control. 2017;6:47. doi: 10.1186/s13756-017-0208-x. PubMed PMID: 28515903; PubMed Central PMCID: PMC5433038.
8. WHO. Antibiotic resistance: WHO; 2018. Available from: http://www.who.int/mediacentre/factsheets/antibiotic-resistance/en/.
9. Pechere JC. Patients' interviews and misuse of antibiotics. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2001;33 Suppl 3:S170-3. doi: 10.1086/321844. PubMed PMID: 11524715.
10. Arsp Working Group TSLCoM. A multi centre laboratory study of Gram negative bacterial blood stream infections in Sri Lanka. Ceylon Med J. 2013;58(2):56-61. doi: 10.4038/cmj.v58i2.5680. PubMed PMID: 23817934.
11. WHO. Regional Strategy on Prevention and Containment of Antimicrobial Resistance. World Health Organization, Regional Office for South-East Asia,; 2010.
12. Llor C, Bayona C, Hernandez S, Moragas A, Miravitlles M. Comparison of adherence between twice- and thrice-daily regimens of oral amoxicillin/clavulanic acid. Respirology. 2012;17(4):687-92. doi: 10.1111/j.1440-1843.2012.02159.x. PubMed PMID: 22390206.
13. Ho1 J, Taylor2 DM, Cabalag1 MS, Ugoni1 A, Yeoh2 M. Factors that impact on emergency department patient compliance with antibiotic regimens. Emergency Medicine Journal. 2010; 27(11).
14. Jin J, GE S, V MSO, S. CL. Factors affecting therapeutic compliance: A review from the patient's perspective. Ther Clin Risk Manag. 2008;4(1):269-86. doi: 10.2147/tcrm.s1458. PubMed Central PMCID: PMC18728716.
15. King C, Nightingale R, Phiri T, Zadutsa B, Kainja E, Makwenda C, et al. Non-adherence to oral antibiotics for community paediatric pneumonia treatment in Malawi - A qualitative investigation. PloS one. 2018;13(10):e0206404. doi: 10.1371/journal.pone.0206404. PubMed PMID: 30379968; PubMed Central PMCID: PMC6209296.
16. Tong S, Pan J, Lu S, Tang J. Patient compliance with antimicrobial drugs: A Chinese survey. American journal of infection control. 2018;46(4):e25-e9. doi: 10.1016/j.ajic.2018.01.008. PubMed PMID: 29592834.
17. Gualano MR, Gili R, Scaioli G, Bert F, Siliquini R. General population's knowledge and attitudes about antibiotics: a systematic review and meta-analysis. Pharmacoepidemiology and drug safety. 2015;24(1):2-10. doi: 10.1002/pds.3716. PubMed PMID: 25251203.
18. Sclar DA, Tartaglione TA, Fine MJ. Overview of issues related to medical compliance with implications for the outpatient management of infectious diseases. Infectious agents and disease. 1994;3(5):266-73. PubMed PMID: 7866659.
19. Hazir T, Fox LM, Nisar YB, Fox MP, Ashraf YP, MacLeod WB, et al. Ambulatory short-course high-dose oral amoxicillin for treatment of severe pneumonia in children: a randomised equivalency trial. Lancet. 2008;371(9606):49-56. doi: 10.1016/S0140-6736(08)60071-9. PubMed PMID: 18177775.
20. Reyes H, Guiscafre H, Munoz O, Perez-Cuevas R, Martinez H, Gutierrez G. Antibiotic noncompliance and waste in upper respiratory infections and acute diarrhea.

Journal of clinical epidemiology. 1997;50(11):1297-304. PubMed PMID: 9393386.
21. Rajesh SM, Singhal V. Clinical Effectiveness of Co-trimoxazole vs. Amoxicillin in the Treatment of Non-Severe Pneumonia in Children in India: A Randomized Controlled Trial. International journal of preventive medicine. 2013;4(10):1162-8. PubMed PMID: 24319556; PubMed Central PMCID: PMC3843303.
22. Baguley D, Lim E, Bevan A, Pallet A, Faust SN. Prescribing for children - taste and palatability affect adherence to antibiotics: a review. Archives of disease in childhood. 2012;97(3):293-7. doi: 10.1136/archdischild-2011-300909. PubMed PMID: 22088684.
23. Madhushani SA, Kommalage M. Use of antibiotics for patients presenting with symptoms suggestive of upper respiratory tract infections of less than 3 days to an outpatient department of a tertiary hospital in Sri Lanka. Sri Lanka Journal of Medicine. 2019;28(1). doi: 10.4038/sljm.v28i1.119.
24. Tillekeratne LG, Bodinayake CK, Nagahawatte A, Vidanagama D, Devasiri V, Arachchi WK, et al. An under-recognized influenza epidemic identified by rapid influenza testing, southern Sri Lanka, 2013. Am J Trop Med Hyg. 2015;92(5):1023-9. doi: 10.4269/ajtmh.14-0708. PubMed PMID: 25732679; PubMed Central PMCID: PMC4426559.
25. Lorenc L, Branthwaite A. Are older adults less compliant with prescribed medication than younger adults? Br J Clin Psychol. 1993;32(4):485-92. Epub 1993/11/01. doi: 10.1111/j.2044-8260.1993.tb01084.x. PubMed PMID: 8298546.
26. Menzies R, Rocher I, Vissandjee B. Factors associated with compliance in treatment of tuberculosis. Tuber Lung Dis. 1993;74(1):32-7. Epub 1993/02/01. doi: 10.1016/0962-8479(93)90066-7. PubMed PMID: 8495018.
27. Centre for Health Protection HK. General Public's Knowledge, Attitude and Practice Survey on Antimicrobial Resistance 2016/17: Centre for Health Protection, Hong Kong. Available from: https://www.chp.gov.hk/en/static/51310.html.
28. André M, Vernby Å, Berg J, Lundborg CS. A survey of public knowledge and awareness related to antibiotic use and resistance in Sweden. Journal of Antimicrobial Chemotherapy. 2010; 65(6):1292–6. doi: 10.1093/jac/dkq104. PubMed Central PMCID: PMC20360063.