



Non-Compliance of Patients with Antibiotic Prescriptions

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Abstract: Non-compliance with antibiotic treatment instructions is dangerous in complete cure, increasing treatment costs and increasing the number of resistant microbes. This study aimed to assess adherence to antibiotic treatment and its associated factors in patients after visiting Libyan community pharmacies. A cross-sectional study was conducted on patients who visited community pharmacies in Libya. Several reasons for non-compliance have been reported but the main ones were it is not necessary to continue taking prescribed medications once feeling better (27.3%), polypharmacy (19.6%), fear of medication adverse effects (18.7%) and the duration of antibiotic treatment also increased the risk of non-compliance (15%). Appropriate prescribing strategies to increase the public awareness, knowledge, and attitude to ensure appropriate antimicrobial use and minimize the problem of non-compliance.

عدم امتثال المرضى لوصفات المضادات الحيوية

الكلمات المفتاحية :
مضادات حيوية؛
المقاومة البكتيرية؛
صيدليات المجتمع؛
التزام المريض؛
ليبيا.

المستخلص: يعد عدم الالتزام بتعليمات العلاج بالمضادات الحيوية أمراً خطيراً يؤثر في الشفاء التام، مما يؤدي إلى زيادة تكاليف العلاج وزيادة عدد الميكروبات المقاومة. هدفت هذه الدراسة إلى تقييم مدى الالتزام بالعلاج بالمضادات الحيوية والعوامل المرتبطة به لدى المرضى بعد زيارتهم الصيدليات المجتمعية. أجريت دراسة بمراقبة المرضى الذين زاروا الصيدليات المجتمعية في ليبيا. تم الإبلاغ عن عدة أسباب لعدم الامتثال ولكن أهمها أنه ليس من الضروري الاستمرار في تناول الأدوية الموصوفة بمجرد الشعور بالتحسن (27.3%)، كما أدى تعدد الأدوية (19.6%) والخوف من الآثار الضارة للأدوية (18.7%) ومدة العلاج بالمضادات الحيوية (15%) إلى زيادة احتمال عدم الامتثال. التركيز على استراتيجيات وصف مناسبة لزيادة الوعي العام والمعرفة والسلوك لضمان الاستخدام المناسب لمضادات الميكروبات وتقليل مشكلة عدم الامتثال.

INTRODUCTION

Medical adherence (or compliance) is defined as the extent to which a patient takes medication as prescribed by their health care providers (Llor et al., 2013) In clinical setting it is important for the patient to adhere to prescribed medications. Non-adherence to antibiotics has led to antimicrobial resistance,

treatment failure, re-infection, which may create a subsequent require for more aggressive treatments and an elevated costs of care, hospitalization and increased risk of mortality (French, 2005) (Bruyndonckx et al., 2021). Non-adherent patients may show primary or secondary non-adherence. Primary non adherence, in which the prescribed medication is not dispensed or never taken,

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the focus of this study will be on the secondary non adherence, in which patients discontinue taking a medication after starting, without being advised by a health care provider (Jimmy & Jose, 2011). Unlike medicines that only individually harm the patient if used inappropriately, misuse of antibiotics can affect others by growing risks within the community and even worldwide to antibiotics resistance (Thorpe et al., 2018).

Non-adherence to antibiotic treatment for acute community infections with respect to short term antibiotic treatment, were reported globally with significant variation among countries ranged from 44.0% in China to 9.9% in the Netherlands (Pechère et al., 2007). There are several identified variables behind non-adherence to antibiotics, these include factors associated with; 1) medication (such as daily dosage regimen), 2) patients attitudes to doctors (patient-physician relationship) and ,3) patients attitudes to antibiotics (knowledge and beliefs) (Fernandes et al., 2014). The above percentages are considered rather high and sound the alarm and the urgent need to perform similar studies to know the rates of compliance with antibiotic treatment in the Libyan society, as Libya was not included in this regard. Importantly, Libya was found to have a significant rate of antibiotic resistance (Shailabi et al., 2022), and antibiotics were widely prescribed with noticeable non-adherence to medication (Mohammed et al., 2016) (Ahmed Atia & Abired, 2017) (Ahmed Atia et al., 2018)

A Libyan study reported higher frequency of inappropriate use of antibiotics for the treatment of undiagnosed diseases with a higher prevalence of bacterial resistance, where the community pharmacists dispensed more antibiotics than general practitioners (Ahmed Atia & Abired, 2017). Another national survey in Benghazi, Libya reported that, medical and nonmedical students had antibiotics without doctor's prescription, just

by purchasing in consultation with a pharmacist, with non-adherence to the enclosed leaflet instructions of the antibiotics or took it to ailments that do not require taking antibiotics such as acne (Ghaieth et al., 2015).

In a survey of antibiotic prescribing practices by doctors in Libya, 18% stated that they may prescribe antibiotics in their prescriptions even if they know that the case is not really in need. The majority of those prescribers justified this practice due to the request of patients (Elbabour et al., 2018). In a study conducted at Abusetta hospital in Tripoli, Libya, the antibiotic resistance pattern of bacteria, exhibited resistance to commonly used antibiotics and to at least one antibiotic (Ahmed Atia, Elyounsi, et al., 2020).

Aim: This study aimed to determine the percentage of adherence to a prescribed antibiotic regimen and is considered one of the first studies to explore the potential factors associated with non-adherence to antibiotics in patients after visiting community pharmacies in Libya.

MATERIALS AND METHODS

A cross-sectional study was conducted on a selected sample of patients who visited community pharmacies across Libya. A sample of 83 pharmacies was randomly selected from those licensed to operate by the Libyan authorities to provide pharmaceutical services in 9 different cities. The study was conducted after approval from the Scientific Research Ethics Committee (SREC), Faculty of Dentistry, Benghazi University, Libya (No, 0107) Written approval (Informed consent) was obtained from all study participants.

Eligible pharmacy customers for the study were those ages ranging from 18 and above, who attended the registered community pharmacies, in the 9 cities representing different parts of the country, between January 2022, and September 2022. Those who presented a prescription for an oral

antibiotic (tablet or capsule) for short-term treatment (less than 30 days) were illegible and included.

Data collection: The questionnaire was structured into five parts: 1) demographic data ,2) the prescribed antibiotic, including the name and dose of the drug, the number of units delivered to the patient, the dosing frequency, and the treatment duration 3) Reasons for giving treatment to the patient, 4) have you adhered to the prescribed antibiotic period? 5) Reasons for non-compliance.

The first three parts of the questionnaire were filled in the pharmacy as general information, the treatment completion date was estimated using collected information. Patients were contacted by phone after the end of the treatment period in order to complete the questionnaire.

Data collected during this interview includes the demographic information: age, gender, level of education, marital status, employment status, and family income. Reasons for prescribed antibiotic treatment for the patient: infection with dental and oral, respiratory system, reproductive system, skin and tissues, ear and eyes, etc.

Factors associated with non-adherence to antibiotic include: 1) Taking many types of drugs, forgetting the correct order and dosage, 2) Pharmacists do not specify the method of administration and dose, 3) Difficulty with taking the antibiotic(non-acceptable smell or shape), 4) Long-term treatment, 5) Concern about the adverse effects described in the medication guide, 6) Antibiotic prices too expensive, 7) Too busy with study or work, 8) Less confidence in doctors, 9) Do not know the exact effect of the prescribed medication,10) insufficient knowledge about the disease and passively taking medication, 11) appearance of an allergy or any side effects after taking the drug, 12) Patients consider that their disease does not require medicine, and will recover on their own,13) Medicine information leaflets are too

scientific to understand,14) Difficult to comply with prescribed doses (e.g., need to break the tablet into two parts), 15) It is not necessary to continue the prescribed medications once they feel better, 16) Deceit and follow advertising television or promotion of other products, 17) The prescribed drug has been changed by the doctor, 18) Lack of care or attention from family members, 19) Preference for herbal medicine/traditional medicine recipes, 20) sudden social events 21) Participants were also asked to state any other reasons for non-compliance were not mentioned in the questionnaire and In addition, participants were allowed to choose multiple answers for non-adherence reasons.

Preliminary pilot testing and subsequent revisions from experts were conducted to check the reliability and validity of the questionnaire with a sample size of 49 participants before starting the study.

RESULTS

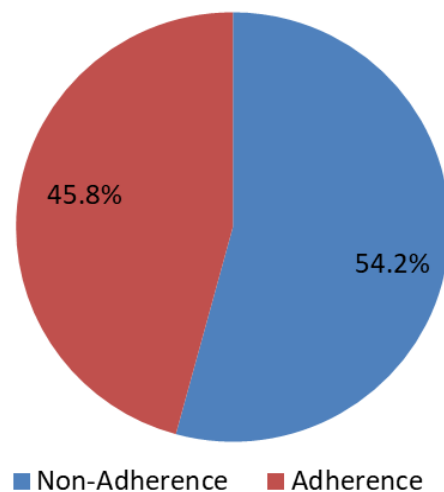


Figure: (1). Proportion of adherence (n = 189) and non-adherence (n = 224) to a prescribed antibiotic regimen among the participants (n 413).

Table:(1). Distribution of Drug Non-Adherence Level Based on Demographic Variables (224 out of 413)

Variables	Drug Adherence (n = 189)	Drug Non-Adherence (n = 224)
Age		
18-24	45(23.8%)	64 (28.5%)
25-34	69(36.5%)	78 (34.8%)
35-44Y	47(24.8%)	47 (21%)
45-54	25(13.2%)	30 (13.4%)
> 54	3(1.6%)	5 (2.2%)
Gender		
Male	58(30.7%)	76 (33.9%)
Female	131(69.3%)	148 (66.1%)
Level Of Education		
Primary school	3(1.6%)	3 (1.3%)
Middle school	5(2.6%)	8 (3.5%)
Secondary school	23(12.2%)	34 (15.2%)
University and above	158(83.6%)	179 (80%)
Marital Status		
Single	74(39.1%)	106(47.3%)
Married	115(60.9%)	118(52.7%)
Employment Status		
Employed	121(64%)	135 (60.3%)
Unemployed	61(32.3%)	79 (35.3%)
Retired	7(3.7%)	10 (4.4%)
Family Income LYD		
750 or less	54(28.6%)	84 (37.5%)
751-1500	74(39.1%)	88 (39.3%)
> 1501-3000	45(23.8%)	42 (18.75%)
3001 or more	16(8.5%)	10 (4.45%)

DISCUSSION

The development of bacterial resistance to antibiotics is mainly caused by the inappropriate use of antibiotics, which helps the emergence and spread of resistant bacteria. The resistance development could result in many consequences. A major consequence is that the infection becomes more difficult or even impossible to treat, sometimes turning a common infection into a life-threatening one (Ahmed, 2020) and (World Health Organization, 2012).

Participants in this study reported several reasons for non-compliance but the main reasons were “it is not necessary to continue taking prescribed medications once they feel better” (27.3%), a similar reason was recently reported in a study conducted by (Elzahaf et al., 2021), revealed significant low knowledge, bad attitude and incorrect practice regarding antibiotics use among the Libyan population. where, they also failed to take a full dose, and they directly stopped taking the course of antibiotics once they felt well. Furthermore, (Tong et al., 2018) found that (41.90%) of the participants reported that they didn't need to continue the antimicrobial therapy once symptoms improved.

Polypharmacy was the second most common cause which is “Taking many types of drugs, forgetting the correct order and dosage” (19.6%), and this complexity of the treatment was also reported as a major cause in Chinese community, where 40.5% did not comply to antimicrobial therapy because they took too many drugs varieties (Tong et al., 2018). Polypharmacy was also the main therapy-related factors that had the potential to decrease the adherence to short-term antibiotics with (61.7%) in a recent Jordanian study (Almomani et al., 2022). Nevertheless, polypharmacy could play a negative role in the adherence to the prescribed medications, where the non-polypharmacy patients were significantly more adherent to prescribed

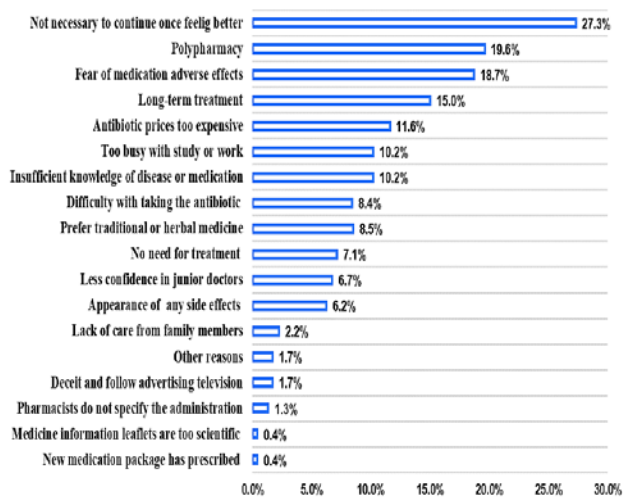


Figure: (2). Reasons for non-adherence to antibiotic therapy

medications than the polypharmacy group (Mohammed et al., 2016).

Fear of adverse effects caused by antibiotic treatment was also noticed as a major cause for non-compliance (18.7%), this fear has been reported in the previous studies with almost 30% (Ahmed, 2020). Additionally, fear of adverse effects is reported as a patient-related factor of non-adherence to short-term antibiotics in adult participants (Almomani et al., 2022). Furthermore, fear of adverse effect again was among the main reasons attributed to poor compliance to antimicrobial therapy in a Chinese study (Tong et al., 2018). Being the fourth highest cause for non-adherence to short-term antibiotics with 15%, the duration can increase the risk of non-adherence, and these findings are consistent with other studies in this regard (Kardas, 2002) and (Fernandes et al., 2014).

The results also showed that the difficulty of purchasing antibiotics due to high prices increased the risk of non-adherence to antibiotics (11.6%), which is consistent with the results of other previous studies (Pechère et al., 2007) and (Kardas, 2002). Practitioners could enhance adherence by emphasizing the value of a patient's regimen and by prescribing and dispensing less expensive medications. Less than one tenth of non-adherents were observed when patients reported difficulty with taking the antibiotic as well as preferring to take traditional or herbal medicine instead. Difficulty with taking the antibiotics were also described in previous researches (Kardas, 2002). This stresses the need to improve antibiotic formulation in order to improve adherence.

Less confidence in junior doctors (6.7%) has been observed to increase the risk of non-adherence to antibiotics, and this finding can be justified by the study conducted on a sample of Junior doctors, employed at primary health centers in the city of Tripoli, Libya, showed that their ready knowledge about proper prescribing of medicines is

insufficient and development in prescribing skills is required (Ahmed Atia, Zanned, et al., 2020).

Participants receiving once-daily regimens (42.0%) were more compliant than those receiving twice (25.6%), three times (31.4%) or four times daily regimens (1.1%), which is similar to previous results reported by (Falagas et al., 2015). Similarly, this observation is in accordance with the finding by (Llor et al., 2013) where adherence was inversely related with the daily number and the duration of antibiotics.

Medicines in Libya can be easily obtained without a prescription. This may lead to misuse, unnecessary risk for patients and could promote the development and spread of antibiotic resistance, (Ahmed Atia, 2020a) reported, in 2020, that the self-medication use of medicines among the Libyan population is widespread and involves antibiotics in high proportion in 7 Libyan cities .

A systematic review showed that, it is a common behavior among the general population to request antibiotic prescriptions from physicians (Duan et al., 2021). (Ahmed Atia, 2018), reported that 56.19% of young Libyans bought their antibiotics without a prescription, among them, 98.1% did not use antibiotics for a full treatment period (< 3 days) or at inappropriate dosing intervals. Another national study performed in Al-Bayda, Libya in 2021 reported that 77.3% of participants disposed of their unused medications in the rubbish, which had almost 40% of the uncompleted antibiotic therapy, the misuse of antibiotics by humans and animals is accelerating the process of resistance to antibiotics (Shailabi & Akrim, 2021)

STUDY LIMITATIONS

The study sample may not represent the entire population, as it mainly includes females and participants with a higher educational level. It

is recommended that further studies be conducted to explore other reasons of non-adherence, and that a national study be conducted on awareness of the proper use of antibiotics and the relationship between non-adherence and antimicrobial resistance to antibiotics.

CONCLUSION

It can be concluded from the results that the level of non-adherence to antibiotic treatment was significant in this study. Physicians, pharmacists and nurses should be deeply involved in training all patients to adhere to the treatment regimen. The importance of this study was to provide real data on patients' adherence to prescribed antibiotic treatment, this is to be used as a tool for evaluating public health strategies aimed at reducing antibiotic resistance and improving antibiotic prescribing as well as its effects on healthcare resource use and costs.

Duality of interest: The authors declare that they have no duality of interest associated with this manuscript.

Author contributions: Taher, Elham, Nisreen and Nagat designed the study. Taher, Elham, and Nisreen collected the data. all authors contributed to interpretation the data. Taher, and Elham drafted the manuscript and revised context and all authors contributed to the final version of the manuscript. Taher supervised the project.

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REFERENCES

Ahmed, N. J. (2020). The Rate of Adherence to Antibiotics and Reasons for Non-adherence among the Public. *Journal of Pharmaceutical Research International*, 32(7), 42–47. <https://doi.org/10.9734/jpri/2020/v32i730458>

Almomani, B. A., Hijazi, B. M., Awwad, O., & Khasawneh, R. A. (2022). Prevalence and predictors of non-adherence to short-term antibiotics: A population-based survey. *PLoS ONE*, 17(5 May), 1–11. <https://doi.org/10.1371/journal.pone.0268285>

Atia, Ahmed. (2018). Monitoring the Level of antibiotic purchase without a prescription among Libyan young adults. *Indian Journal of Pharmacy Practice*, 11(4), 208–211. <https://doi.org/10.5530/ijopp.11.4.43>

Atia, Ahmed. (2020a). Epidemiology of Self-Medication Practice among Libyans: A Systematic Review and Meta-Analysis. *Preprints*, June, 1–9. <https://doi.org/10.20944/preprints202006.0335.v1>

Atia, Ahmed, Abired, A., Ammar, A., Elyounsi, N., & Ashour, A. (2018). Prevalence and types of bacterial infections of the upper respiratory tract at a tertiary care hospital in the City of Tripoli. *Libyan International Medical University Journal*, 3(2), 54. https://doi.org/10.4103/liuj.liuj_23_18

Atia, Ahmed, Elyounsi, N., Abired, A., Wanis, A., & Ashour, A. (2020). Antibiotic resistance pattern of bacteria isolated from patients with upper respiratory tract infections; a four-year study in Tripoli city. *Iberoamerican Journal of Medicine*, 03(August), 155–160. <https://doi.org/10.20944/preprints201808.0435.v1>

Atia, Ahmed, Zanned, S., & Bakait, N. (2020). *Exploring the Ready Knowledge of Drug Prescribing among Junior Doctors in Libya*. 2020–2023. <https://doi.org/10.4103/LJMS.LJMS>

Atia, AhmedE, & Abired, A. (2017).

- Antibiotic prescribing for upper respiratory tract infections by Libyan community pharmacists and medical practitioners: An observational study. *Libyan Journal of Medical Sciences*, 1(2), 31. https://doi.org/10.4103/ljms.ljms_14_17
- Bruyndonckx, R., Adriaenssens, N., Versporten, A., Hens, N., Monnet, D. L., Molenberghs, G., Goossens, H., Weist, K., & Coenen, S. (2021). Consumption of antibiotics in the community, European Union/European Economic Area, 1997-2017: Data collection, management and analysis. *Journal of Antimicrobial Chemotherapy*, 76, II2–II6. <https://doi.org/10.1093/jac/dkab171>
- Duan, L., Liu, C., & Wang, D. (2021). The general population's inappropriate behaviors and misunderstanding of antibiotic use in China: A systematic review and meta-analysis. *Antibiotics*, 10(5). <https://doi.org/10.3390/antibiotics10050497>
- Elbabour, F., Benkhaial, A., & Elemam, R. Antibiotic Prescribing Practices in Libya: A cross-sectional Survey.
- Elzahaf, R. A., Rabeea, A. A., Mohamed, F. A., Ramadan, S., Fadhlalla, A., Alkhawwajah, T. A., & Shaheen, M. K. (2021). Knowledge, Attitude and Practice Regarding to Antibiotics use among Libyan Community. *Saudi J Med Pharm Sci*, 4929, 599–608. <https://doi.org/10.36348/sjumps.2021.v07i12.002>
- Falagas, M. E., Karagiannis, A. K. A., Nakouti, T., & Tansarli, G. S. (2015). Compliance with once-daily versus twice or thrice-daily administration of antibiotic regimens: A meta-analysis of randomized controlled trials. *PLoS ONE*, 10(1), 1–15. <https://doi.org/10.1371/journal.pone.0116207>
- Fernandes, M., Leite, A., Basto, M., Nobre, M. A., Vieira, N., Fernandes, R., Nogueira, P., & Jorge, P. (2014). Non-adherence to antibiotic therapy in patients visiting community pharmacies. *International Journal of Clinical Pharmacy*, 36(1), 86–91. <https://doi.org/10.1007/s11096-013-9850-4>
- French, G. L. (2005). Clinical impact and relevance of antibiotic resistance. *Advanced Drug Delivery Reviews*, 57(10), 1514–1527. <https://doi.org/10.1016/j.addr.2005.04.005>
- Ghaieth, M. F., Elhag, S. R. M., Hussien, M. E., & Konozy, E. H. E. (2015). Antibiotics self-medication among medical and nonmedical students at two prominent Universities in Benghazi City, Libya. *Journal of Pharmacy and Bioallied Sciences*, 7(2), 109–115. <https://doi.org/10.4103/0975-7406.154432>
- Jimmy, B., & Jose, J. (2011). Patient medication adherence: Measures in daily practice. *Oman Medical Journal*, 26(3), 155–159. <https://doi.org/10.5001/omj.2011.38>
- Kardas, P. (2002). Patient compliance with antibiotic treatment for respiratory tract infections. *Journal of Antimicrobial Chemotherapy*, 49(6), 897–903. <https://doi.org/10.1093/jac/dkf046>
- Llor, C., Hernández, S., Bayona, C., Moragas, A., Sierra, N., Hernández, M., & Miravittles, M. (2013). A study of adherence to antibiotic treatment in ambulatory respiratory infections. *International Journal of Infectious Diseases*, 17(3), 168–172.

<https://doi.org/10.1016/j.ijid.2012.09.012>

Mohammed, M. A., Alnour, T. M. S., Shakurfo, O. M., & Aburass, M. M. (2016). Prevalence and antimicrobial resistance pattern of bacterial strains isolated from patients with urinary tract infection in Messalata Central Hospital, Libya. *Asian Pacific Journal of Tropical Medicine*, 9(8), 771–776. <https://doi.org/10.1016/j.apjtm.2016.06.011>

Health Affairs, 37(4), 662–669. <https://doi.org/10.1377/hlthaff.2017.1153>

Tong, S., Pan, J., Lu, S., & Tang, J. (2018). Patient compliance with antimicrobial drugs: A Chinese survey. *American Journal of Infection Control*, 46(4), e25–e29. <https://doi.org/10.1016/j.ajic.2018.01.008>

Organization, W. H. (2012). The evolving threat of antimicrobial resistance: Options for action. *WHO Publications*, 1–119. www.who.int/patientsafety/en/%0Ahttp://www.ijmr.org.in/article.asp?issn=0971-5916;year=2014;volume=139;issue=1;spage=182;epage=183;aulast=Kapi

Pechère, J. C., Hughes, D., Kardas, P., & Cornaglia, G. (2007). Non-compliance with antibiotic therapy for acute community infections: a global survey. *International Journal of Antimicrobial Agents*, 29(3), 245–253. <https://doi.org/10.1016/j.ijantimicag.2006.09.026>

Shailabi, T., Aldeeb, O. H., Almaedani, A. F., Borwis, E. O., & Amer, S. A. (2022). Antimicrobial Susceptibility Patterns of *Escherichia coli* from Urine Isolates. *Al-Mukhtar Journal of Sciences*, 37(4), 372–384.

Shailabi, T. I. M., & Akrim, Z. S. M. (2021). Disposal Methods of Expired and Unused Medications among the General Public in Al-Bayda City. *Al-Mukhtar Journal of Sciences*, 36(3), 209–215. <https://doi.org/10.54172/mjsc.v36i3.337>

Thorpe, K. E., Joski, P., & Johnston, K. J. (2018). Antibiotic-resistant infection treatment costs have doubled since 2002, now exceeding \$2 billion annually.