ORIGINAL ARTICLE

Antibiotic Prescribing and Use

INTERNATIONAL
JOURNAL
OF BIOMEDICINE

Prevalence of Antibiotic Prescription in Primary Healthcare Settings in the Municipality of Prishtina, Kosovo

Valon Krasniqi[1], Elton Bahtiri[1*], Flaka Pasha[1], Vjollca Zeqiri[2], Sami Uka[2], Peter Zarb[3],
Lul Raka[4,5], Hasime Qorraj Bytyqi[1], Blana Krasniqi[6]

[1]Department of Pharmacology and Toxicology and Clinical Pharmacology,
University of Pristina "Hasan Prishtina," Prishtina, Kosovo
[2]Main Family Medical Centre, Prishtina, Kosovo
[3]Department of Pathology, University of Malta, Msida, Malta
[4]Department of Microbiology, University of Pristina "Hasan Prishtina," Prishtina, Kosovo
[5]National Institute of Public Health, Prishtina, Kosovo
[6]Faculty of Medicine, Tirana Medical University, Tirana, Albania

Abstract

Background: Antibiotics remain among the most prescribed drugs in primary healthcare, contributing to increased antibiotic resistance in the community and prevailing as an emerging global health concern. We aimed to quantify the prevalence and quality of antibiotic prescription in primary healthcare settings in the Municipality of Prishtina to identify targets for quality improvement.

Methods and Results: This study represents a population-based, retrospective cohort, including data from eight randomly selected family medical centers in the Municipality of Prishtina. Each 150th patient on medical records was assessed for demographic data, diagnosis (ICD-10), antibiotic prescription, antibiotic class, and antibiotic form. In total, the study included 1614 cases reviewed. The antibiotic prescription rate was 16%. The health condition for which most of the cases received antibiotics was J18 - Pneumonia, unspecified organism (67%), followed by J03 - Acute tonsillitis (54%), J42 - Unspecified chronic bronchitis (46%), and N39 - Other disorders of the urinary system (43%). Broad-spectrum antibiotics, such as co-amoxiclav (17.7%), amoxicillin (16.5%), and ceftriaxone (12.6%), featured among the most routinely prescribed antibiotics. The antibiotic prescription rate was the highest for cases in the 3-5 age group, of whom 27% received an antibiotic prescription. In 73% of cases, oral antibiotics were prescribed, 69% of which belong to the WHO AWaRe (Access, Watch, Reserve) essential medicines list. Only 18% of antibiotics were prescribed with their generic names.

Conclusion: The prevalence of antibiotic prescription in primary healthcare settings in Prishtina is moderately low. These data cannot be extrapolated to other municipalities in Kosovo or other countries due to different organizational levels. High antibiotic prescription rates for young age groups, prescription of broad-spectrum antibiotics, and high rates of parenteral antibiotics were identified as targets for quality improvement.**(International Journal of Biomedicine. 2024;14(1):134-140.)**

Keywords: antibiotic prescription • primary healthcare • antibiotic resistance • Kosovo

Introduction

Kosovo, with a population of 1.7 million inhabitants, is located in southeast Europe in the Western Balkans region. To date, Kosovo lags in the establishment of a health insurance system and electronic medical records, which highly influence the real documentation of epidemiological situations or antibiotic prescription rates. Life expectancy at birth is 71 years, and communicable diseases are still among the largest ongoing healthcare problems.[1]

For decades, antibiotics have been crucial in decreasing the morbidity and mortality burden of infectious diseases.[2] There is robust evidence emphasizing that there is little to no clinical benefit from antibiotic treatment for the most common respiratory tract infections, which are usually self-limiting and often caused by viruses.[3] Yet antibiotics remain among

the most prescribed drugs in primary healthcare settings for acute sinusitis, acute pharyngitis, acute bronchitis, nonspecific upper respiratory tract infections, and the common cold.[4]

Prescribing antibiotics to patients increases the risk of side effects, encourages help-seeking behavior, and increases antibiotic resistance in the community.[5] Patients treated with first-line antibiotics can become colonized by resistant bacteria, especially in the first weeks after treatment, which may persist for up to 12 months.[6] Such patients are at a greater risk of infection with resistant bacteria. In recurrent infections, the likelihood of being prescribed second-line antibiotics increases, thereby increasing the population effect of community antibiotic resistance.[7] Furthermore, many doctors do not link antibiotic resistance with their prescribing attitude and consider it a more general issue.[8] Developing effective interventions will require increased knowledge of the mechanisms that underlie these predictors of inappropriate antibiotic prescribing.[9] Although antibiotic prescription in primary care settings has decreased by about a third in most developed countries,[10] the use of broad-spectrum agents has steadily increased.[11] The greatest concern related to excessive broad-spectrum antibiotic prescription in primary healthcare settings remains its continuous contribution to increasing antibiotic resistance globally.[12]

Urinary tract infections are among the most common infections in primary healthcare settings. Countrywide comparative results of the resistance rate among *Escherichia coli* isolates analyzed between 2004 and 2016 showed a significant increase. Resistance to aminopenicillins increased from 40.2% to 75.3%, and ciprofloxacin from 2.6% to 29.4%.[13] Therefore, antimicrobial resistance is one of the major challenges for the healthcare system in Kosovo. The main challenges in this area also remain the inappropriate use of antibiotics, lack of officially approved clinical guidelines and protocols, "over-the-counter sale" of antimicrobials, and strong pressure from the pharmaceutical industry.[14]

The primary healthcare system in Kosovo provides initial diagnoses and patient care for 80%-90 % of the cases, thus acting as gatekeepers for secondary and tertiary healthcare.[15] Primary healthcare services are decentralized to the municipality level, increasing liability and service quality. Yet, primary healthcare is not equally developed and organized in all municipalities.[16] Family medical centers in Kosovo are responsible for diagnosing and curative care, including minor surgery and drug management; immunization; emergency care and stabilization of emergency patients; maternal and child healthcare; reproductive health services, including antenatal and post-natal care, as well as family planning and treatment of sexually transmitted diseases. All primary healthcare facilities in Prishtina offer laboratory services and functional advanced equipment. They also offer public accountability items, guidelines, and information materials for their patients.[17]

Primary healthcare settings of Prishtina have one main Family Medicine Center, which consists of 31 family medicine centers (Table 1). These primary healthcare centers cover Prishtina's entire urban and rural areas, comprising more than 200 thousand inhabitants. During 2017, family medical centers of Prishtina offered over one million medical consultations and 2.4 million other medical services.[18]

Recalling the large number of medical consultations and services offered in primary care settings of the Municipality of Prishtina, with this study we aimed to quantify the percentage of antibiotic prescriptions and quality of antibiotic prescriptions in primary healthcare settings in the Municipality of Prishtina for 2017. Additionally, reducing antibiotic prescriptions at the general practice level was associated with reduced local antibiotic resistance. Therefore, we will use our findings to encourage clinicians to prescribe antibiotics conservatively.[19]

Table 1.
Family medical centres in Municipality of Prishtina.

Primary healthcare settings of Prishtina		
QKMF Prishtinë	QMF Mati1	Mirditë
QMF 1 Prishtinë	QMF Mat	Mramur
QMF 2 Prishtinë	QMF Hajvali	Rimanisht
QMF 3 Prishtinë	QMF Besi	Shahskovcë
QMF 4 Prishtinë	QMF Bardhosh	Shkabaj
QMF 5 Prishtinë	Barilevë	Viti
QMF 6 Prishtinë	Bullaj	Sharban
QMF 7 Prishtinë	Slivovë	Qendra e Studenteve
QMF 8 Prishtinë	Keqekollë	
QMF 9 Prishtinë	Kishnicë	
QMF 10 Prishtinë	Koliq	
QMF 11 Prishtinë	Llukar	

Materials and Methods

Study population

This study represents a population-based, retrospective cohort, including data from eight randomly selected family medical centers in the Municipality of Prishtina. By medical center randomization, we achieved a representative sample and avoided bias. Each 150th patient on medical records was assessed for demographic data, diagnosis, antibiotic prescription, antibiotic class, and antibiotic form (if antibiotics were prescribed). In total, the study included 1614 cases reviewed.

Inclusion Criteria: Every doctor who worked in one of these eight randomly selected primary healthcare centers was included in the study. The data for every 150th patient registered on medical records was analyzed, regardless of whether the patient was prescribed antibiotics or not.

Exclusion Criteria: Topical antibiotics (vaginal pessaries, skin preparations, or nasal, ear, and eye preparations) were not included in this survey.

Data collection

Data were collected retrospectively for 12 months, from January 1 to December 31, 2017. A customized questionnaire

was used to collect data, including the patient's registry number, treatment date, demographic data, patient diagnosis (ICD-10), antibiotic brand and generic name, and pharmacologic form. Antibiotic dose and duration of treatment were not included in the study due to the lack of complete data on protocols. To avoid data collection errors, nurses chosen to collect the data were initially trained. In addition, each questionnaire was signed by the nurse who collected the data, thus internal validation could be performed afterwards.

Data analysis

From the data collected with questionnaires, we created a database further analyzed with the statistical software package SPSS version 20.0 (SPSS Inc, Armonk, NY: IBM Corp). The relation between antibiotic prescription rate and other independent variables, like demographic data and patient diagnosis, were analyzed through correlation and variance tests.

Results

The antibiotic prescription rate was 16%. There were major differences in antibiotic prescription rates among the eight primary healthcare centers included in the study, varying from 6.9% up to 20%. Family Medical Centers #9 and #2 had the highest antibiotic prescription rates, 20% and 19.8%, respectively. Conversely, Family Medical Centre #11 had the lowest antibiotic prescription rate, only 6.9% (Figure 1).
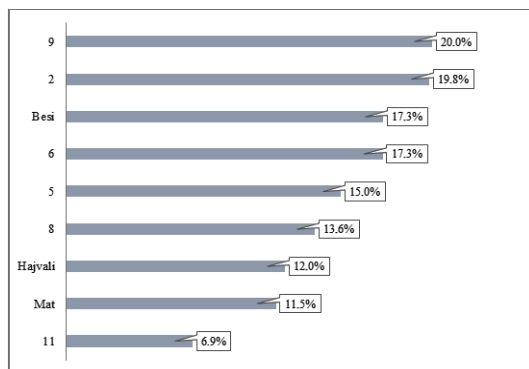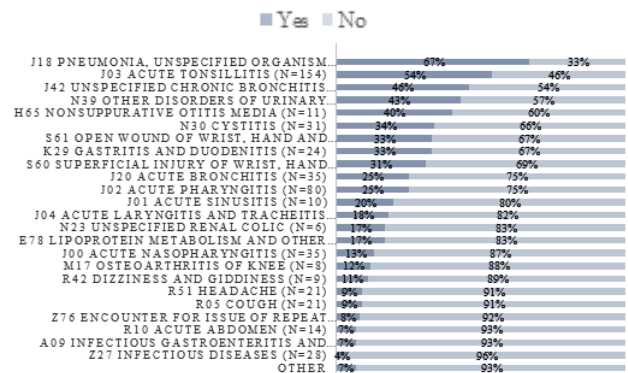

Fig. 1. _Frequency of antibiotic prescription among different primary healthcare centres in Municipality of Prishtina_

The health condition for which most of the cases received antibiotics was J18 - Pneumonia, unspecified organism (67%), followed by J03 - Acute tonsillitis (54%), J42 - Unspecified chronic bronchitis (46%), and N39 - Other disorders of the urinary system (43%) (Figure 2). The "Other" section includes all conditions with five or fewer cases.

Conditions for which antibiotics were not prescribed are depicted below (only conditions with more than 5 cases are included): I10 - Essential hypertension (n=94), J11 - Influenza – unidentified virus (n=23), D50 - Iron deficiency anemia (n=19), E10 - Type 1 diabetes mellitus (n=10), E11 - Type 2 diabetes mellitus (n=20), H10 -Conjunctivitis (n=11), I95 - Hypotension (n=10), M47 - Spondylosis (n=19), M53 - Other and unspecified

dorsopathies, not elsewhere classified (n=6), M54 - Dorsalgia (n=28), M79 - Other and unspecified soft tissue disorders, not elsewhere classified (n=8), R11 - Nausea and vomiting (n=22), Z00 - Encounter for general examination without complaint, suspected or reported diagnosis (n=62), Z01 - Encounter for other special examination without complaint, suspected or reported diagnosis (n=60), Z03 - Encounter for medical observation for suspected diseases and conditions ruled out (n=18), Z34 - Encounter for supervision of normal pregnancy (n=18). Overall, Z76- Encounter for the issue of repeat prescription was the most commonly encountered diagnosis, with 329(20.38%) cases.

Fig. 2. _Frequency of antibiotic prescription for the most common diagnoses based on ICD-10._

Broad-spectrum antibiotics, such as co-amoxiclav (17.7%), amoxicillin (16.5%), and ceftriaxone (12.6%), featured among the most routinely prescribed antibiotics. Amoxicillin featured among the most routinely prescribed antibiotics for J02 - Acute pharyngitis, followed by co-trimoxazole for N30 - Cystitis and co-amoxiclav for Z76 - Encounter for issues of repeat prescription. Conditions with 5 cases or below were not included (Figure 3).
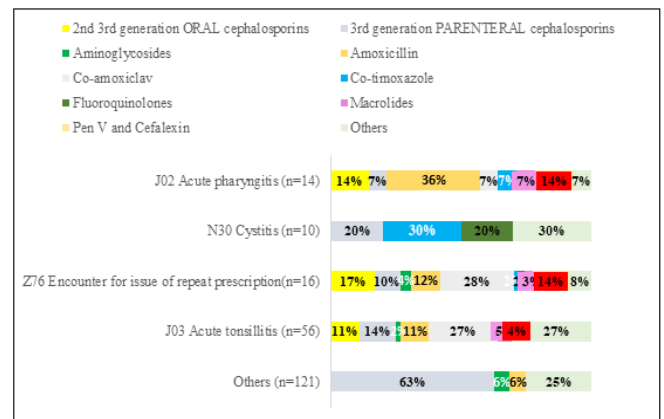
Fig. 3. _The most common prescribed antibiotics in primary healthcare settings in Prishtina by diagnosis._

The antibiotic prescription rate was the highest for cases in the 3-5 age group, of whom 27% received an antibiotic prescription. This group was followed by the 6-9 age group (21.6%) and the 19-29 age group (21.6%). The 10-14 age group (20%) also was above the general average of 16% (Figure 4a).
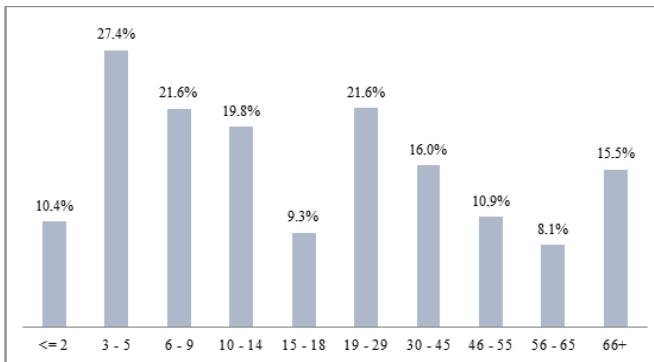
Fig. 4a. *The frequency of antibiotic prescription among different age groups.*

The frequency of groups of antibiotics was assessed for different age groups. While co-amoxiclav is the most frequently prescribed antibiotic for younger age groups, its peak prescription period being for the 15-18 age group, it seems to reduce as individuals get older. The most frequently prescribed antibiotics among older age groups are second- and third-generation oral cephalosporins (Figure 4b).
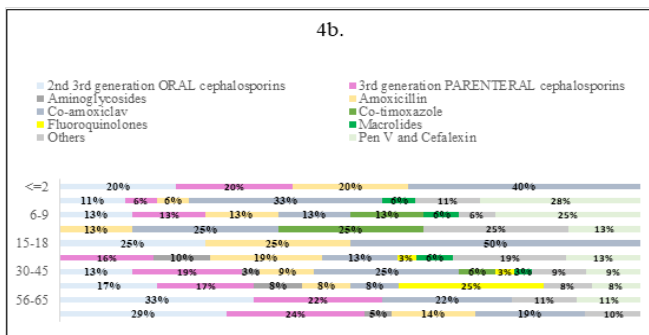

Fig. 4b. *The frequency of antibiotic group prescription among different age groups.*

In addition, we observed the most common diagnoses encountered in different age groups. The most frequently encountered condition among all age groups was J03 - Acute tonsillitis; however, individuals of older age groups (56+) were more likely to be diagnosed with other conditions (Figure 4c).
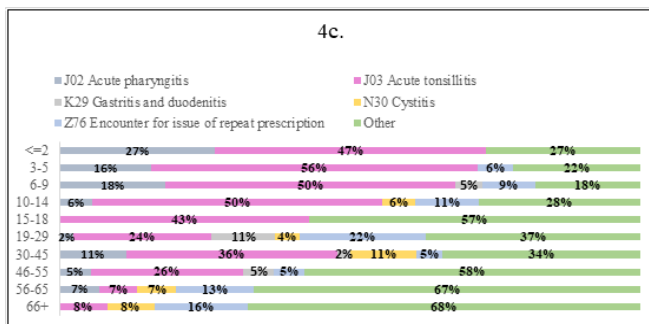

Fig. 4c. *Prevalence of the most common conditions by different age groups.*

Furthermore, we analyzed antibiotic prescription rates among different age groups for the most frequent diagnoses,

namely J02 - Acute pharyngitis, J03 - Acute tonsillitis, and Z76 - Encounter for the issue of a repeat prescription (Figure 5a, 5b, 5c). No significant correlation between these variables was observed.
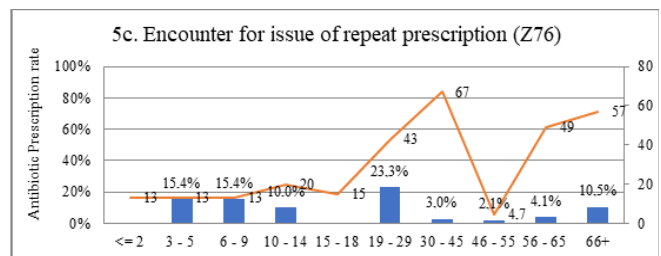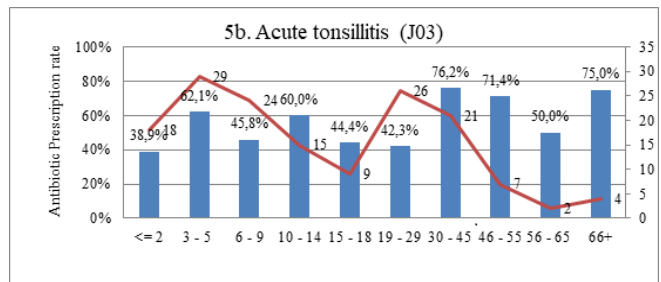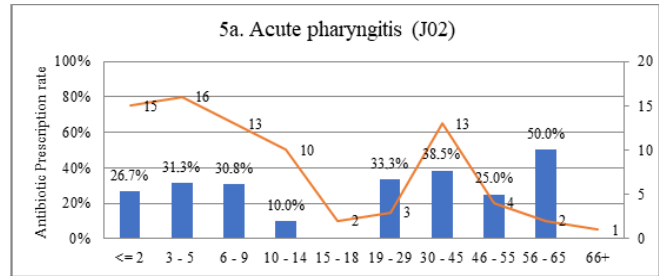

Fig. 5 a.b.c. *The most common conditions by different age groups.*

We further examined whether there was any relation between antibiotic prescription rates for different age groups and genders, mainly focusing on parental pressure for antibiotic prescription to their children or any gender impurities (Figure 6). No significant correlation between antibiotic prescription rates for different age groups and genders were observed.
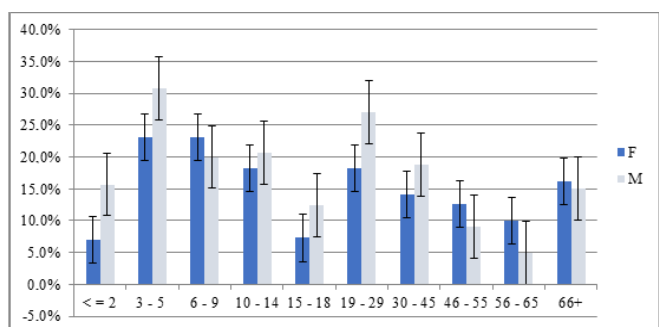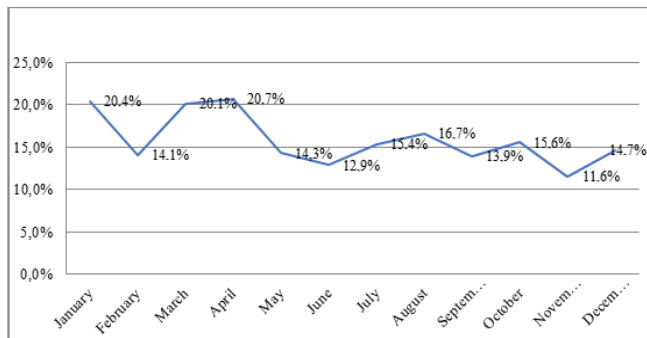

Fig. 6. *Antibiotic prescription rates for different age groups and gender.*

We additionally examined if there was any relation between antibiotic prescription rates through different months or seasons (Figure 7). January (20%), March (20%), and April (21%) had the highest antibiotic prescription rates. In comparison, the antibiotic prescription rate in November was the lowest, only 12%.

Fig. 7. *The frequency of antibiotic prescription among different months/ seasons.*

In 86% of the cases, primary healthcare physicians prescribed antibiotics for their patients. In only 14% of the cases, antibiotics were encountered for issues of repeated prescription based on a previous prescription from a secondary or tertiary specialist. In 73% of cases, oral antibiotics were prescribed, 69% of which belong to the WHO AWaRe essential medicines list. Seventy-six percent of cephalosporins were prescribed by primary care physicians, and the remaining 24% were a repeated prescription from secondary or tertiary care specialists. Cefalexin (3.5%), cefaclor (4.7%), cefixime (6.3%), and ceftriaxone (12.6%) were the most prescribed cephalosporins. Only 18% of antibiotics were prescribed with their generic names. From the oral forms, amoxicillin, co-amoxiclav, and cefaclor were mainly prescribed with their generic names, while from parenteral drugs, gentamicin was only prescribed with its generic name.

Discussion

In low- and middle-income countries like Kosovo, infectious diseases remain among the main reasons for primary care visits, entailing unnecessary antibiotic prescriptions.[20] Antibiotic prescription rates in the Municipality of Prishtina remain moderately low, varying from 6.9% up to 20% in different family medical centers. This result highlights the major differences in antibiotic prescription attitudes of primary care doctors and the lack of officially approved clinical guidelines and protocols that doctors could rely on.[21]

Our study found a high prevalence of antibiotic prescription among young age groups. Most antibiotics, ranging from 20% to 27.4%, were prescribed to children 3-14 years old for acute tonsillitis. Other studies also reveal that 63%-77% of four-year-old children were prescribed antibiotics for acute otitis media in the U.S.[22] or the Netherlands.[23] Additionally, a German national survey revealed increasing antibiotic prescription rates in children and adolescents, specifically for tonsillitis, bronchitis, otitis media, and acute upper respiratory infections.[24] Our study also revealed that the incidence of antibiotic prescription for the 19-29 age group was 21.6%, mostly for acute tonsillitis (24%), and amoxicillin and second- and third-class cephalosporin (19%) were antibiotics of choice. Recalling that antibiotic prescription in the early days of life is highly related to metabolic diseases and being overweight, these findings are concerning.[25] In addition, different studies found that self-limiting respiratory tract infections, such as pharyngitis, were the main reason for antibiotic prescriptions in up to 60% of patients from all age groups.[26] Nevertheless, prescribing antibiotics for self-limiting respiratory tract infections must be intensively monitored, and educational programs to gradually change physicians' attitudes toward antibiotic prescription should be implemented.[27]

Potentially, the lack of etiologic treatment or empirical management of diseases in primary care centers in Prishtina continuously led to the prescription of broad-spectrum antibiotics such as amoxicillin, co-amoxiclav, and ceftriaxone, as we noticed in our study. In addition, other studies revealed that extensive use of broad-spectrum antibiotics leads to antibiotic resistance developing more rapidly in the community.[28] Moreover, in our study, we noticed that 82% of antibiotics were prescribed with their brand names, thus increasing the cost burden for patients and potentially leading to a lack of treatment adherence. This potentially indicates the pharmaceutical industry influences physicians' daily decisions and emphasizes the immediate need for drug- price equalization in the Kosovo market.[29]

Besides, antibiotic prescription rates in outpatient care settings, inappropriate antibiotic selection, dosing, and duration of treatment, as well as increasing antibiotic resistance, remain emerging topics of public health and a national priority in many countries.[30] Of the total antibiotics consumed in the outpatient settings, at least 30% are unnecessary, and 50% of prescriptions are inappropriate concerning drug selection, dosing, and/or duration.[31]

Our study has a few minor limitations due to incomplete protocol data. We could not quantify the antibiotic doses and duration of treatment. We also could not include the number of over-the-counter sales of antibiotics in Prishtina due to the lack of electronic medical records and public health insurance systems. These could be of great interest to investigate in other studies soon.

Surveillance of antibiotic consumption was one of the success stories during the implementation of the first National Strategy and Action Plan (2011-2015) in Kosovo.[32] Data for antibiotic consumption were collected in three levels of health care in Kosovo: wholesale data, data from all hospitals, and data at the primary care level. Wholesale data on antibacterial use in Kosovo was 26.3 DID in 2012.[33] However, the latest WHO publication on antibiotic consumption in Europe, published in December 2018, showed that Kosovo has marked a significant decrease in antibiotic consumption by almost 25%.[34] The main factors influencing this decline in consumption are the increased awareness of the population

and healthcare workers about antimicrobial resistance, media pressure, and governmental commitment to address antimicrobial resistance.

Ceftriaxone was the most prescribed antibiotic in hospitals and at the primary healthcare level. Prescription with generic names was noted only in 31% of cases in primary care. [35]

To address the challenge of antimicrobial resistance, the Ministry of Health initially completed the National Strategy and Action Plan to Combat Antimicrobial Resistance 2011-2015, where 80% of planned activities were successfully implemented. In December 2018, the Minister of Health signed a new action plan for antimicrobial resistance for three years. The new action plan has five strategic objectives and 47 activities. The cornerstone of this action plan will be antimicrobial stewardship. Other action areas will be strengthening the "One Health" approach, improving the surveillance of antimicrobial resistance and antimicrobial consumption in humans, animals, and the environment; prudent use of antimicrobials in clinical practice and the veterinary sector; infection prevention and control in healthcare settings and community; and promotion of research and international cooperation.[36]

To successfully implement national strategies for proper antibiotic use and to rightly address the threat posed by antimicrobial resistance, physicians and patients must have a profound knowledge of the topic. Public health campaigns and treatment guidelines for specific infectious diseases and target groups proved unsuccessful in reducing inappropriate antibiotic prescriptions through the years.[37] Nevertheless, multifaceted interventions—considering infectious diseases in all age groups, vaccination, changing physicians' prescribing behavior, blended learning, and physician-patient shared decision-making—are recently considered the most effective tools to lower antibiotic prescription rates.[38]

Antibiotic optimization may be limited due to social, value-based, and ethical dilemmas, and reducing antibiotic prescription in primary healthcare settings should not imply increased patient revisits or admission to the hospital, thus leading to increased healthcare expenses and overall costs.[39]

Conclusion

We can conclude that antibiotic prescription rates in primary care in Prishtina remain satisfying. Yet these numbers might not reflect the real situation influenced by the lack of electronic medical records and public health insurance systems. Healthcare professionals in Kosovo should adopt antibiotic stewardship recommendations for quality improvement by prescribing antibiotics only when there is a clear clinical benefit, by using simple generic antibiotics and reducing broad-spectrum antibiotic prescription in young age groups, as well avoiding unnecessary antibiotic prescriptions for self-limiting conditions or parenteral forms, avoiding widespread use of topical antibiotics, and finally trying to narrow down and control over-the-counter sale of antibiotics. Finally, developing and monitoring the implementation of clinical guidelines and protocols for antibiotic prescriptions in physicians' daily practice and continuously educating patients on appropriate antibiotic use would further help reduce antibiotic prescription rates and antibiotic resistance in the community.

Competing Interests

The authors declare that they have no competing interests.

References

1. The World Bank. Life expectancy at birth, total (years). Available from: https://data.worldbank.org/indicator/SP.DYN.LE00.IN?locations=XK&view=chart.
2. Teillant A, Gandra S, Barter D, Morgan DJ, Laxminarayan R. Potential burden of antibiotic resistance on surgery and cancer chemotherapy antibiotic prophylaxis in the USA: a literature review and modelling study. Lancet Infect Dis. 2015 Dec;15(12):1429-37. doi: 10.1016/S1473-3099(15)00270-4.
3. Fleming DM, Ross AM, Cross KW, Kendall H. The reducing incidence of respiratory tract infection and its relation to antibiotic prescribing. Br J Gen Pract. 2003 Oct;53(495):778-83.
4. Llor C, Hernández S. Enfermedad infecciosa en atención primaria: estudio prospectivo efectuado durante todo un año [Infectious disease in primary care: 1-year prospective study]. Enferm Infecc Microbiol Clin. 2010 Apr;28(4):222-6. Spanish. doi: 10.1016/j.eimc.2009.03.014.
5. Kristiansson C, Reilly M, Gotuzzo E, Rodriguez H, Bartoloni A, Thorson A, Falkenberg T, Bartalesi F, Tomson G, Larsson M. Antibiotic use and health-seeking behaviour in an underprivileged area of Perú. Trop Med Int Health. 2008 Mar;13(3):434-41. doi: 10.1111/j.1365-3156.2008.02019.x.
6. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ. 2010 May 18;340:c2096. doi: 10.1136/bmj.c2096.
7. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P T. 2015 Apr;40(4):277-83. PMID: 25859123;
8. McCullough AR, Rathbone J, Parekh S, Hoffmann TC, Del Mar CB. Not in my backyard: a systematic review of clinicians' knowledge and beliefs about antibiotic resistance. J Antimicrob Chemother. 2015 Sep;70(9):2465-73. doi: 10.1093/jac/dkv164.
9. Cadieux G, Tamblyn R, Dauphinee D, Libman M. Predictors of inappropriate antibiotic prescribing among primary care physicians. CMAJ. 2007 Oct 9;177(8):877-83. doi: 10.1503/cmaj.070151.
10. Curtis HJ, Walker AJ, Mahtani KR, Goldacre B. Time trends and geographical variation in prescribing of antibiotics in England 1998-2017. J Antimicrob Chemother. 2019 Jan 1;74(1):242-250. doi: 10.1093/jac/dky377.
11. Bätzing-Feigenbaum J, Schulz M, Schulz M, Hering R, Kern WV. Outpatient Antibiotic Prescription. Dtsch Arztebl Int. 2016 Jul 1;113(26):454-9. doi: 10.3238/arztebl.2016.0454.
12. Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S, Rasool MH, Nisar MA, Alvi RF, Aslam MA, Qamar MU, Salamat MKF, Baloch Z. Antibiotic resistance: a rundown of

a global crisis. Infect Drug Resist. 2018 Oct 10;11:1645-1658. doi: 10.2147/IDR.S173867.

13. Ministry of Health, Republic of Kosovo (2018) PLANI STRATEGJIK PËR REZISTENCËN ANTIMIKROBIKE 2019-2021. Available: http://konsultimet.rks-gov.net/viewConsult.php?ConsultationID=40484.

14. Davari M, Khorasani E, Tigabu BM. Factors Influencing Prescribing Decisions of Physicians: A Review. Ethiop J Health Sci. 2018 Nov;28(6):795-804. doi: 10.4314/ejhs.v28i6.15.

15. Mustafa M, Hysa B. Kosovo healthcare system still without consolidated funding! Alban Med J. 2016;1:45-51.

16. Ymerhalili G, Maxhuni B. Integrating Care in Kosovo: challenges for Primary Health Care. International Journal of Integrated Care.2017;17(5):A265.

17. Accessible Quality Healthcare (2018). Primary Health Care in Kosovo. Quality of Care Study. Available: http://www.aqhproject.org/wp-content/uploads/2019/03/AQH-QoC-Prishtin%C3%AB-WEB-4.pdf.

18. Hoxha T. Yearly report of medical visits and services in Main Family Medical Centre of Prishtina (2017). Available: http://www.qkmf-pr.org/prezentimet-dhe-raportet.

19. Butler CC, Dunstan F, Heginbothom M, Mason B, Roberts Z, Hillier S, Howe R, Palmer S, Howard A. Containing antibiotic resistance: decreased antibiotic-resistant coliform urinary tract infections with reduction in antibiotic prescribing by general practices. Br J Gen Pract. 2007 Oct;57(543):785-92.

20. Hamers RL, van Doorn HR. Antibiotic consumption in low-income and middle-income countries. Lancet Glob Health. 2018 Jul;6(7):e732. doi: 10.1016/S2214-109X(18)30270-5. Erratum in: Lancet Glob Health. 2018 Sep;6(9):e967.

21. Ebben RH, Vloet LC, Verhofstad MH, Meijer S, Mintjes-de Groot JA, van Achterberg T. Adherence to guidelines and protocols in the prehospital and emergency care setting: a systematic review. Scand J Trauma Resusc Emerg Med. 2013 Feb 19;21:9. doi: 10.1186/1757-7241-21-9.

22. Shapiro DJ, Hicks LA, Pavia AT, Hersh AL. Antibiotic prescribing for adults in ambulatory care in the USA, 2007-09. J Antimicrob Chemother. 2014 Jan;69(1):234-40. doi: 10.1093/jac/dkt301.

23. Uijen JH, Bindels PJ, Schellevis FG, van der Wouden JC. ENT problems in Dutch children: trends in incidence rates, antibiotic prescribing and referrals 2002-2008. Scand J Prim Health Care. 2011 Jun;29(2):75-9. doi: 10.3109/02813432.2011.569140.

24. Holstiege J, Garbe E. Systemic antibiotic use among children and adolescents in Germany: a population-based study. Eur J Pediatr. 2013 Jun;172(6):787-95. doi: 10.1007/s00431-013-1958-y.

25. Miller SA, Wu RKS, Oremus M. The association between antibiotic use in infancy and childhood overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2018 Nov;19(11):1463-1475. doi: 10.1111/obr.12717.

26. Randel A; Infectious Disease Society of America. IDSA Updates Guideline for Managing Group A Streptococcal Pharyngitis. Am Fam Physician. 2013 Sep 1;88(5):338-40.

27. Roque F, Herdeiro MT, Soares S, Teixeira Rodrigues A, Breitenfeld L, Figueiras A. Educational interventions to improve prescription and dispensing of antibiotics: a systematic review. BMC Public Health. 2014 Dec 15;14:1276.

doi: 10.1186/1471-2458-14-1276.

28. Palumbi SR. Humans as the world's greatest evolutionary force. Science. 2001 Sep 7;293(5536):1786-90. doi: 10.1126/science.293.5536.1786.

29. Souliotis K, Papageorgiou M, Politi A, Athanasiadis A. Pharmaceutical Pricing Policy in Greece: Toward a Different Path. Front Public Health. 2016 Aug 31;4:185. doi: 10.3389/fpubh.2016.00185.

30. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. Pathog Glob Health. 2015;109(7):309-18. doi: 10.1179/2047773215Y.0000000030.

31. CDC: 1 in 3 antibiotic prescriptions unnecessary. (2016) Available from: https://www.cdc.gov/media/releases/2016/p0503-unnecessary-prescriptions.html

32. European Centre for Disease Prevention and Control. Strategies and action plans on antimicrobial resistance. Available from: http://www.euro.who.int/__data/assets/pdf_file/0010/378361/68wd08e_I_PR_AMR_180421.pdf?ua=1

33. Versporten A, Bolokhovets G, Ghazaryan L, Abilova V, Pyshnik G, Spasojevic T, Korinteli I, Raka L, Kambaralieva B, Cizmovic L, Carp A, Radonjic V, Maqsudova N, Celik HD, Payerl-Pal M, Pedersen HB, Sautenkova N, Goossens H; WHO/Europe-ESAC Project Group. Antibiotic use in eastern Europe: a cross-national database study in coordination with the WHO Regional Office for Europe. Lancet Infect Dis. 2014 May;14(5):381-7. doi: 10.1016/S1473-3099(14)70071-4.

34. World Health Organization. WHO Report on Surveillance of Antibiotic Consumption: 2016–2018 early implementation. Available from: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://eody.gov.gr/wp-content/uploads/2019/01/who_amr_amc_report_20181109.pdf

35. Krasniqi S, Versporten A, Jakupi A, Raka D, Daci A, Krasniqi V, Deva Z, Rashiti A, Brajshori N, Hajdari S, Bytyqi J, Neziri B, Goossens H, Raka L. Antibiotic utilisation in adult and children patients in Kosovo hospitals. Eur J Hosp Pharm. 2019 May;26(3):146-151. doi: 10.1136/ejhpharm-2017-001363.

36. Raka L, Kurti A, Jakupi A, Krasniqi S, Turjaka A. Kosovo's national action plan for antimicrobial resistance. Lancet Infect Dis. 2019 Mar;19(3):244. doi: 10.1016/S1473-3099(19)30052-0.

37. Sabuncu E, David J, Bernède-Bauduin C, Pépin S, Leroy M, Boëlle PY, Watier L, Guillemot D. Significant reduction of antibiotic use in the community after a nationwide campaign in France, 2002-2007. PLoS Med. 2009 Jun 2;6(6):e1000084. doi: 10.1371/journal.pmed.1000084.

38. van Esch TEM, Brabers AEM, Hek K, van Dijk L, Verheij RA, de Jong JD. Does shared decision-making reduce antibiotic prescribing in primary care? J Antimicrob Chemother. 2018 Nov 1;73(11):3199-3205. doi: 10.1093/jac/dky321.

39. Broom J, Broom A, Good P, Lwin Z. Why is optimisation of antimicrobial use difficult at the end of life? Intern Med J. 2019 Feb;49(2):269-271. doi: 10.1111/imj.14200.

*Corresponding author: Prof. Assoc. Dr. Elton Bahtiri MD, PhD. Department of Pharmacology and Toxicology and Clinical Pharmacology, University of Prishtina "Hasan Prishtina", Prishtina, Kosovo. E-mail: elton.bahtiri@uni-pr.edu