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Antibiotic use in a district hospital in Kabul, Afghanistan: are we overprescribing?

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Setting: A district hospital in Kabul, Afghanistan, supported by Médecins Sans Frontières (MSF).
Objectives: To assess antibiotic prescribing practices in the out-patient department in summer (August 2013) and winter (January 2014).
Design: Cross-sectional study, using routinely collected hospital data and using World Health Organization (WHO) defined daily dose (DDD) methodology.
Results: An analysis of 4857 prescriptions (summer) and 4821 prescriptions (winter) showed that respectively 62% and 50% of all out-patients were prescribed at least one antibiotic. Prescriptions without a recorded diagnosis represented a sizeable proportion of all antibiotics prescribed. For upper respiratory tract infections (URTI), dental indications, urinary tract infections (UTI) and diarrhoea, good adherence to dosages recommended in the MSF standard treatment guidelines was observed when measured by DDD. However, certain drugs not indicated in the guidelines were prescribed, such as amoxicillin and metronidazole for UTI and azithromycin for URTI.
Conclusion: Rates of antibiotic prescriptions for out-patients in a district hospital in Afghanistan were high, double the WHO recommendation of 30%. While systematic non-adherence to recommended dosages was not observed, inappropriate prescriptions for specific conditions may have occurred. This study suggests that knowledge about context-specific determinants of antibiotic prescribing is a first step towards promoting rational prescribing practices in such settings.

Rational prescription of medications is important to ensure optimal use of resources, foster effective therapy and minimise side effects.[1,2] In practice, one of the most common irrational uses of medicines is excessive prescription of antimicrobials.[3] Antimicrobials are often overused for minor infections, misused for viral infections in the case of antibiotics, and may be over- or underused due to financial or availability constraints.[4] Such misuse is a key driver of antimicrobial resistance, and poses a threat to public health by increasing the complexity and cost of treatment and reducing the probability of successful patient outcomes. According to a recent report by the World Health Organization (WHO) on antimicrobial resistance, death from an infectious illness is twice as likely to occur when a resistant bacteria is the causative pathogen.[5] In the same report, the WHO estimated alarming rates of resistance in bacteria causing common hospital and community acquired infections in all WHO regions.[5] Evidence from ecological studies in Europe, using the WHO anatomical therapeutic classification/defined daily dose (ATC/DDD) methodology as an indicator for drug consumption across geographical areas and services, demonstrated a positive correlation between out-patient antibiotic use and antibiotic resistance.[6]

Médecins Sans Frontières (MSF), an international medical humanitarian organisation, has developed standard treatment guidelines to promote rational drug use to improve clinical management and facilitate staff training and drug forecasting. In Kabul, Afghanistan, MSF supports the Ahmed Shah Baba (ASB) district hospital, including the management of the out-patient department (OPD). Over-consumption of antibiotics is a realistic threat in aid-supported settings such as Afghanistan, and may be linked to the observed high prevalence of antibiotic resistance there.[7,8] Nevertheless, an assessment of antibiotic utilisation and prescribing practices has not been reported in out-patient facilities in Afghanistan, or in similar humanitarian-run facilities. We therefore conducted an analysis of the antibiotic prescribing practices in this hospital.

Specifically, the study was undertaken to determine 1) the frequency of antibiotic prescriptions; 2) for selected diagnoses, what proportion of patients received an antibiotic; 3) for selected antibiotics, proportions per diagnosis; and 4) adherence to MSF treatment guidelines based on the DDD methodology. The DDD is defined as the assumed average maintenance dose per day for a given drug used for its main indication in adults[9] (Table).

METHODS

Design

This cross-sectional study used routinely collected hospital out-patient data.

Setting

Located in South Asia, with a population of approximately 30 million and a gross national income per capita of US$680,[10] Afghanistan is a country that has been ravaged by conflict for several decades. This has greatly undermined health services delivery and led to a virtual absence of public health facilities. It is not surprising, therefore, that Afghanistan has some of the poorest health indicators in the world with, for example, an estimated maternal mortality ratio of 400 per 100 000 live births.[11] In addition, communicable diseases continue to dominate as the leading cause of morbidity and mortality, accounting for 60–80% of

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TABLE ATC/DDD methodology used to assess adherence of antibiotic prescribing to MSF treatment guidelines, in a district hospital, Kabul, Afghanistan

For each of the selected diagnoses — dental use, urinary tract infection, upper respiratory tract infection and diarrhoea — the maximum daily dosages of the antibiotics as recommended by the MSF treatment guidelines were converted to DDDs using WHO ATC/DDD formula.
DDD = quantity (number of dose units of a defined strength x conversion factor).
From the collected data of out-patients, each antibiotic prescribed for each selected diagnosis was converted to DDDs using the same WHO ATC/DDD formula.
An average of total DDDs for each antibiotic prescribed for the population of each diagnosis was calculated.
The average DDDs prescribed for each antibiotic for each diagnosis was compared with the calculated standard DDDs.

ATC/DDD = anatomical therapeutic classification/defined daily dose; MSF = Médecins Sans Frontières; WHO = World Health Organization.

out-patient visits at any health facility.[12] The top six diseases reported in out-patient clinics in 2007 in Afghanistan were acute respiratory infections (ARIs), diarrhoeal diseases, urinary tract infections (UTI), trauma, psychiatric disorders and suspected tuberculosis (TB) cases.[13] Afghanistan ranks 175th of 186 countries on the human development index, and was the fourth largest recipient of official humanitarian assistance, amounting to US$6.5 billion, in 2011.[14]

ASB district, one of 20 districts in Kabul province, is located in the outskirts of Kabul and is surrounded by many small villages. The district community has been expanding rapidly over the last 10 years due to the arrival of returnees from Pakistan and Iran and internally displaced persons (IDPs) from insecure areas in Afghanistan. Today, the district has an estimated 264 000 inhabitants. In 2009, MSF, in collaboration with the Ministry of Public Health (MoPH) in Afghanistan, started to support the ASB Centre, which was later upgraded to a district hospital in 2010; it is the only public hospital in the district.

With a capacity of 68 beds, the ASB hospital has in-patient wards for surgery, maternity, paediatric and internal medicine. In addition, the hospital has an emergency department, an operating theatre, a dental clinic and an OPD. Laboratory and X-ray services are all available at the hospital. There is also a central pharmacy. The OPD is one of the busiest departments in the hospital, averaging 7500 consultations per month. Consultation services include general OPD, wound dressing, antenatal and postnatal care, post-surgical follow-up and family planning. The top three diagnoses recorded in the OPD are upper respiratory tract infection (URTI), diarrhoea and UTI, with diarrhoea being more common in summer. Chronic diseases such as hypertension and diabetes account for on average 1% of consultations. Patients attending the hospital are first triaged by nurses: those who are triaged to the OPD and are prescribed medications by a dentist or physician obtain them from the dispensary located inside the hospital premises. The dispensary supplies only oral medications. The MSF ASB Central Pharmacy supplies the dispensary. There are nine MoPH doctors, all trained in standard MSF treatment guidelines. All services in the hospital are provided free of charge.

Study population

The study included all adult patients (aged ⩾15 years) who attended the OPD of the ASB hospital and received a prescription during the months of August 2013 (summer period) and January 2014 (winter period).

Variables and data collection

The source of the data was the prescriptions of adult patients received in the dispensary. The ATC/DDD of the specific antibiotic under study was obtained from the WHO ATC/DDD index 2014.[6]

Analysis and statistics

We used EpiData software for data entry (v3.1, EpiData Association, Odense, Denmark) and analysis (v2.2.2.182). The DDDs for each antibiotic were calculated using the WHO formula for daily dose calculation: quantity x conversion factor.[15]

For the most prevalent conditions, diarrhoea, URTI, UTI and dental consultations, the total dosage (expressed as a DDD) of each antibiotic recommended by the MSF standard treatment guidelines[16] was calculated. Lower respiratory tract infections (LRTI) were excluded from this analysis, as patients often receive an intravenous (IV) loading dose of antibiotic, and the oral continuation doses are highly variable, depending on when IV administration was suspended. Subsequently, the total prescribed dosage regimen of each drug per consultation was calculated as a population average (expressed as DDD), and was compared to the total recommended dosage regimen per consultation. In the case of multiple conditions per consultation, it was impossible to trace for which condition each antibiotic was prescribed. Such cases represented 6% of all patients receiving an antibiotic.

Ethics

The study was approved by the Institutional Review Board (IRB) of Afghanistan National Public Health Institute (ANPHI), Ministry of Public Health, Kabul, Afghanistan and met the approval criteria of the Ethics Review Board of Médecins Sans Frontières (Geneva, Switzerland) for analysis of routinely collected programme data. It also satisfied the requirements of the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France.

RESULTS

Antibiotic prescription frequency

In the OPD of the ASB hospital, 4857 prescriptions for adults in the summer period and 4821 in the winter period were analysed. One prescription equates to one

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Conflicts of interest: none declared.

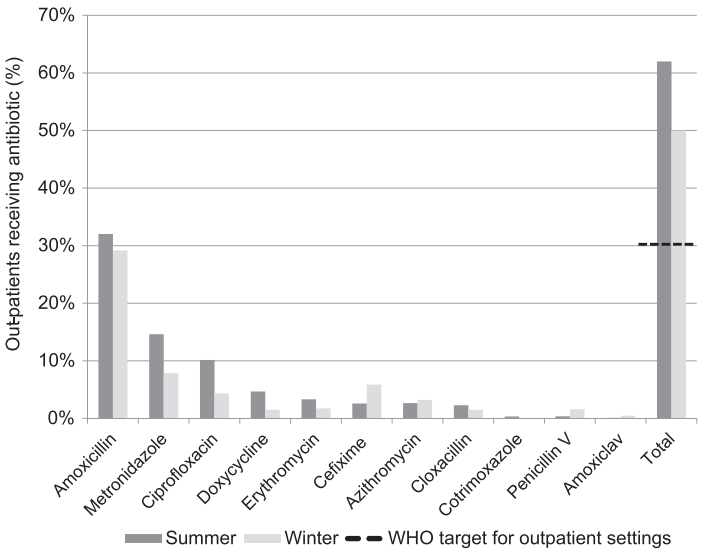

FIGURE 1 Proportion of out-patients receiving antibiotics during one month in summer (August 2013) and winter (January 2014) in a district hospital, Kabul, Afghanistan. WHO = World Health Organization.

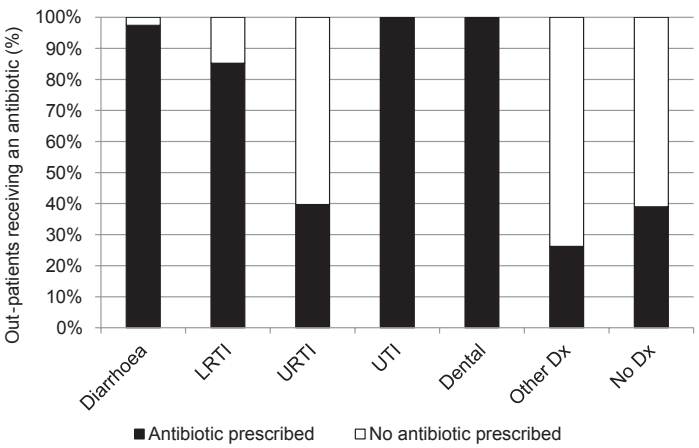

FIGURE 2 Proportion of out-patients with a selected diagnosis receiving an antibiotic in winter (January 2014) in a district hospital, Kabul, Afghanistan. LRTI = lower respiratory tract infection; URTI = upper respiratory tract infection; UTI = urinary tract infection; Dx = diagnosis.

adult out-patient receiving zero to several antibiotics. Seventy-one percent of the total out-patient population was female, and the median age was 35 years (IQR 23–45). In the summer and winter months, respectively 62% and 50% of all prescriptions were for an antibiotic. The distribution of prescribed drugs is shown in Figure 1: amoxicillin use was the highest, at respectively 32% and 29% in summer and winter. Metronidazole was the second most prescribed antibiotic in both months, followed by ciprofloxacin. Antibiotic prescription rates per diagnosis in the winter period are shown in Figure 2. They could not be assessed in the summer period, as total diagnoses were not collected in this period. The antibiotic prescription rates were highest for patients with UTI (100%), for those with a dental consultation (100%) and for diarrhoea (97%). Among patients with URTI and those without a registered diagnosis, 40% received an antibiotic.

Antibiotic use by diagnosis

The proportion of all patients receiving each selected antibiotic per diagnosis is shown in Figure 3. In both summer and winter, 'diagnosis not recorded' accounted for the highest proportion of amoxicillin prescribed, at 49% and 55%, respectively. Azithromycin was indicated for respectively 49% and 40% of all URTIs in summer and winter.

Adherence to MSF standard treatment guidelines using DDD methodology

The average prescribed total dosage (expressed as DDDs) of antibiotics corresponded relatively well to the maximum DDD-expressed dosages indicated by the standard MSF treatment guidelines **(**Figure 4**)**, although inappropriate use (over-prescription) at the individual patient level cannot be excluded. However, some antibiotics were prescribed for conditions for which they were not indicated in the guidelines, such as erythromycin and metronizadole for dental use and amoxicillin and metronizadole for UTI.

DISCUSSION

To the best of our knowledge, this is the first study to assess overall antibiotic use for multiple diagnoses in an out-patient facility in a district hospital in Afghanistan. It complements an audit conducted to assess antibiotic use prevalence for ARIs over a 6-day period in an Afghan clinic run by Kinderberg International (KBI) providing emergency primary care, which found that 47% of all patients received an antibiotic and 75% of patients diagnosed with an ARI were prescribed an antibiotic.[17]

Our investigation revealed two key findings. First, a high proportion of out-patients were prescribed an antibiotic in both seasons, with amoxicillin, metronidazole and ciprofloxacin being most commonly prescribed. The rate in summer represented double the WHO recommendation of 30%[18] for antibiotic use in out-patient settings and was two-thirds higher in winter. However, our findings seem to be consistent with antibiotic rates reported in other studies conducted in lower- and middle-income countries (LMICs) such as Nigeria, Zimbabwe and Pakistan, which have reported antibiotic use in out-patients ranging from 50% to 57%.[19] Similarly, in China, a systematic review found that on average half of all out-patients across the country were prescribed an antibiotic.[20] We note that a physician was employed by MSF to work on improving the overall quality of OPD consultations, and new medical records and prescriptions were implemented between October 2013 and January 2014. This may partially explain why there was a 12% decrease in antibiotic prescriptions in winter compared to summer. Second, our analysis suggests that among the drugs prescribed per diagnosis, the average dosage adhered to the maximum total dosage (expressed as DDD) recommended in the MSF treatment guidelines. There does not therefore seem to be systematic non-adherence to recommended dosages.

The high proportion of patients receiving an antibiotic may be due to inappropriate prescribing behaviour. In winter, almost all diarrhoea patients and almost half of URTI patients were prescribed an antibiotic, even though, in general, 60% of all acute, watery diarrhoea cases and most URTIs have viral causes and are thus unresponsive to antibiotic treatments.[16] Furthermore, all patients who attended a dental consultation received an antibiotic, consistent with a recent review of studies worldwide on dental prescribing practices, also suggesting potential over-prescribing.[21] Overall, the Centers for Disease Control and Prevention (CDC, Atlanta, GA, USA) estimate that one third of all dental antibiotics

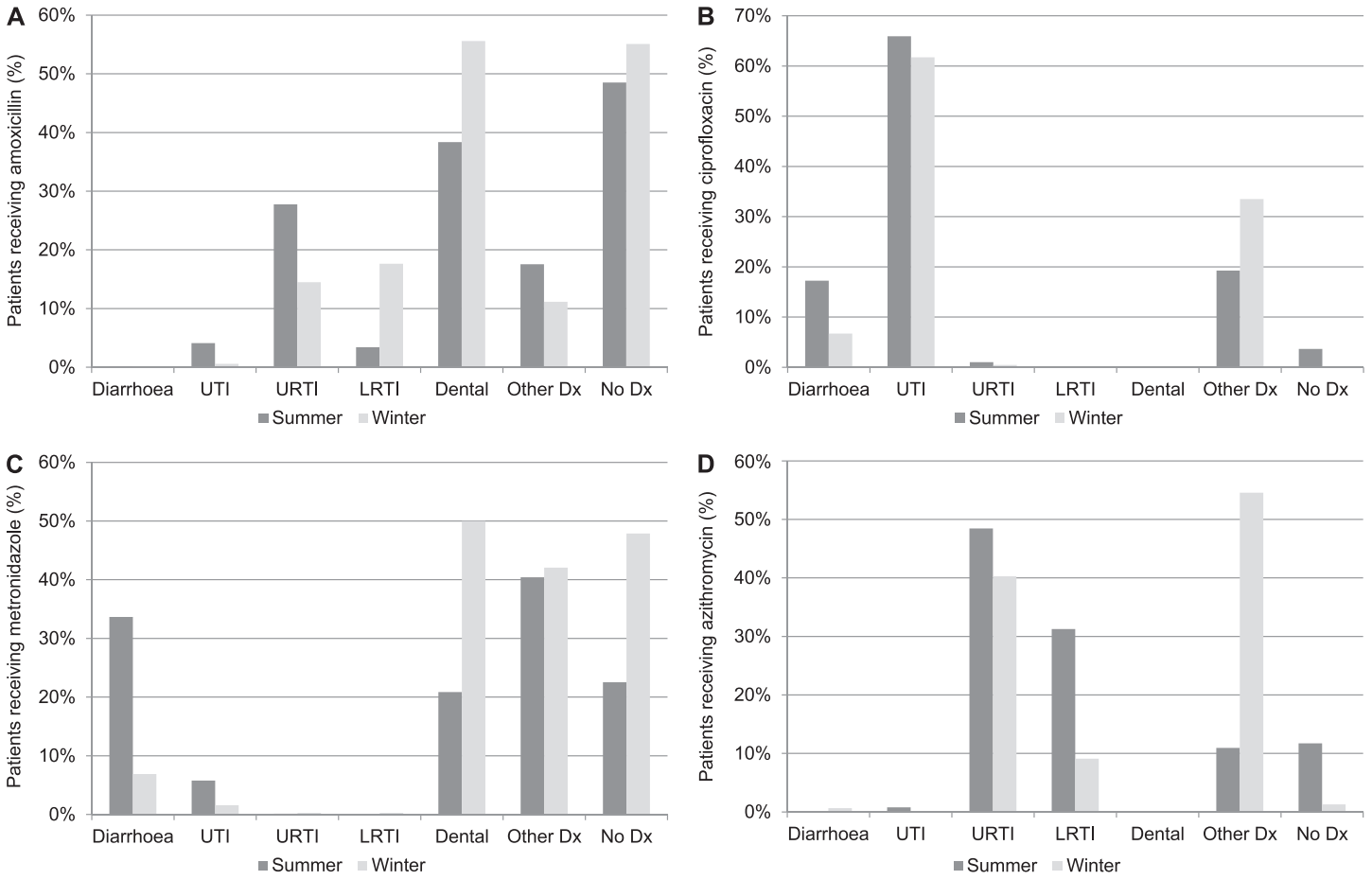

FIGURE 3 Proportion of selected antibiotics (**A)** amoxicillin, **B)** ciprofloxacin, **C)** metronidazole, **D)** azithromycin) prescribed for specific diagnoses in summer (August 2013) and winter (January 2014), in a district hospital, Kabul, Afghanistan. UTI = urinary tract infection; URTI = upper respiratory tract infection; LRTI = lower respiratory tract infection; Dx = diagnosis.

prescribed in out-patient settings are unnecessary; this may also be true in our setting.[21] The high rate of antibiotics prescribed for patients without a registered diagnosis may be the consequence of poor registration of diagnoses, or may reflect 'compassionate' use of antibiotics, where drugs were prescribed at the request of a patient without a true indication. In addition, potential irrational choices of specific antibiotics were noted: for example, erythromycin and metronidazole were used for dental use, which does not correspond to the MSF guidelines, and the prescription of amoxicillin and metronidazole for UTI may also indicate potential irrational use. Similarly, a very high proportion of azithromycin was prescribed for URTI, indicating potential irrational use. Taken together, our findings suggest a potentially systematic inappropriate choice of antibiotics, but among the antibiotics prescribed (appropriately or not), the dosages were generally in accordance with the standard treatment guidelines.

Antibiotic overuse and resistance are increasing global health concerns. While our findings suggest higher rates of antibiotic prescription than recommended by the WHO in out-patient settings, they resemble those of other studies conducted in similar resource-limited settings.[4,20] This thus raises the question as to whether context-specific determinants of antibiotic use should be considered in resource-limited settings. For example, patients in resource-limited settings probably attend hospitals when they are more ill than those in industrialised countries, and antibiotics may be more appropriate at a later stage of the disease. Family members may also attend the OPD on behalf of patients who are unable to attend, to request antibiotics. Similarly, distance, difficulties with transport and other socio-economic factors may prevent patients from returning to the OPD if their condition worsens. Doctors may thus feel obliged to prescribe antibiotics in case their condition worsens. In addition to such pressure or expectations of patients to obtain antibiotic prescriptions, other context-specific determinants of antibiotic over-prescription could be poor knowledge of clinical guidelines and/or of antibiotic resistance,[19] limited consultation times (5–7 min), and lack of knowledge on or access to antibiotic susceptibility and diagnostic information, leading to diagnoses being made empirically. Furthermore, as a humanitarian organisation-supported hospital, medications are provided free of charge, and prescriptions may therefore be given with less hesitation. Understanding such context-specific antibiotic prescription practices is vital if we are to move forward in the global fight against antibiotic resistance.

There are a number of strengths to this study. A large number of prescriptions were collected and analysed from the representative months of summer and winter, thereby reducing seasonal bias. The study adhered to strengthening the reporting of observational studies in epidemiology (STROBE) guidelines,[22] and the MSF standard treatment guidelines were used to assess adherence to dosage recommendations. Trained staff with pharmaceutical

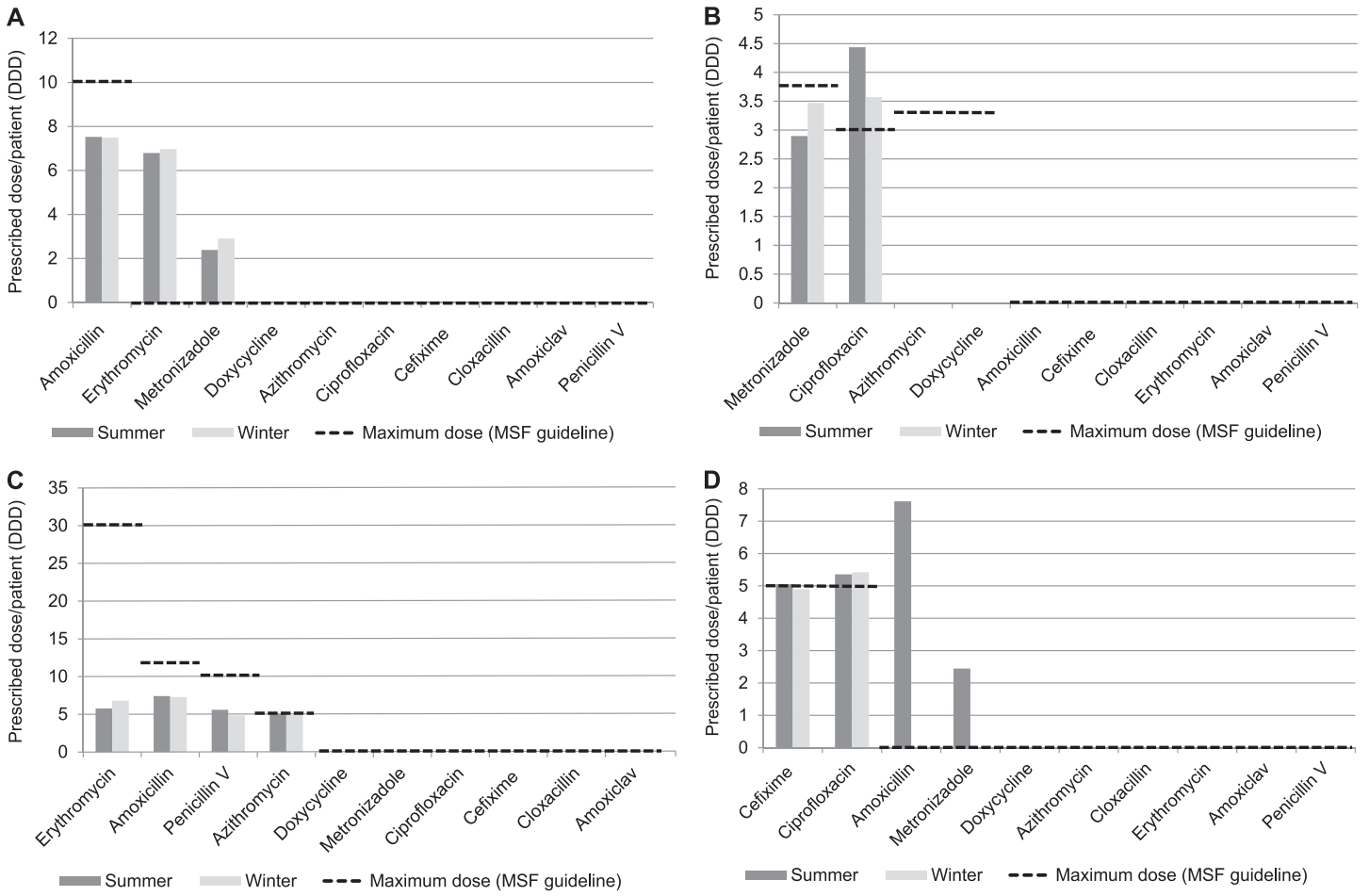

FIGURE 4 Average defined daily dose per antibiotic in summer (August 2013) and winter (January 2014) in a district hospital, Kabul, Afghanistan. **A)** Dental, **B)** diarrhoea, **C)** URTI, **D)** UTI. DDD = defined daily dose; MSF = Médecins Sans Frontières; URTI = upper respiratory tract infection; UTI = urinary tract infection.

experience performed data encoding, reducing the likelihood of encoding errors. All antibiotics in the study were available (i.e., no stock-outs) in the OPD.

Our study also has some limitations. First, we could not assess the appropriateness of the selection of the antibiotics prescribed, as we were unable to confirm the empiric diagnoses. In addition, the ATC/DDD methodology is designed to assess population aggregated data and not those at individual level. However, we feel confident that for the use described here, relying on limited programme data, the methodology is adequate to assess adherence to the dosages recommended in our setting. Finally, in patients with multiple conditions, it was impossible to assess the condition the antibiotic was prescribed for, and all diagnoses were analysed as separate conditions. However, as such cases were limited in number, this is unlikely to have influenced the results.

In conclusion, the frequency of antibiotic prescriptions was high among out-patients attending a district hospital in Afghanistan; systematic over-dosage did not appear to be a concern, but inappropriate prescription/drug selection may have occurred systematically. Our study, along with others from LMICs, suggests that the context may need to be considered when recommendations are made as regards appropriate prescribing of antibiotics. With more detailed knowledge of context and patterns of non-adherence to standard treatment guidelines, rational prescribing may be promoted and antibiotic resistance reduced.

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Contexte : Un hôpital de district à Kaboul, Afghanistan, soutenu par Médecins Sans Frontières (MSF).
Objectifs : Evaluer les pratiques en matière de prescription d'antibiotiques en consultation externe en été (août 2013) et en hiver (janvier 2014).
Schema : Etude transversale basée sur les données hospitalières recueillies en routine et la méthode de dose thérapeutique quotidienne (DDD) de l'Organisation Mondiale de la Santé (OMS).
Resultats : L'analyse de 4857 prescriptions (été) et de 4821 prescriptions (hiver) a montré que respectivement 62% et 50% de tous les consultants externes se voyaient prescrire au moins un antibiotique. Les prescriptions non accompagnées d'un diagnostic établi représentaient une proportion importante de l'ensemble des antibiotiques prescrits. En ce qui concerne les infections respiratoires hautes (URTI), les problèmes dentaires, les infections urinaires (UTI) et la diarrhée, on notait une bonne adhésion aux doses recommandées dans les directives standard de traitement de MSF quand on les mesurait en fonction des DDD. Cependant, certains médicaments, ne figurant pas dans les directives, étaient néanmoins prescrits comme par exemple l'amoxicilline et la métronidazole dans les UTI et l'azithromycine dans les URTI.
Conclusion : Les taux de prescriptions d'antibiotiques en consultation externe dans un hôpital de district d'Afghanistan étaient très élevés, atteignant le double des recommandations de l'OMS de 30%. Même s'il n'a pas été observé de non adhésion aux doses recommandées, il semble y avoir eu des prescriptions inappropriées pour certaines pathologies. Cette étude suggère que la connaissance des déterminants de la prescription d'antibiotiques en fonction du contexte est une première étape dans la rationalisation des pratiques de prescription dans ce type de situation.

Marco de referencia: Un hospital distrital de Kabul en Afganistán, que cuenta con el respaldo de Médecins Sans Frontières.
Objetivos: Evaluar las prácticas en materia de formulación de antibióticos en el servicio ambulatorio durante el verano (agosto del 2013) y el invierno (enero del 2014).
Método: Fue este un estudio transversal a partir de la información hospitalaria recogida de manera sistemática, mediante la aplicación del sistema de clasificación anatómica terapéutica química y dosis diaria definida (ATC/DDD) de la Organización Mundial de la Salud (OMS).
Resultados: Al analizar las 4857 recetas del verano y las 4821 recetas del invierno, se puso en evidencia que 62% de los pacientes ambulatorios durante el verano y 50% de los pacientes durante el invierno recibían una receta como mínimo con un antibiótico. En una proporción considerable de todas las recetas con antibióticos, no existía un diagnóstico asociado registrado. Se observó un cumplimiento adecuado de las dosis recomendadas en las infecciones de las vías respiratorias superiores, las indicaciones odontológicas, las infecciones del tracto urinario y la diarrea, al comparar las directrices de tratamiento de Médecins Sans Frontières con las medidas DDD. Sin embargo, se recetaron algunos medicamentos que no estaban indicados en las directrices, como la amoxicilina y el metronidazol en casos de infección de las vías urinarias y la azitromicina en casos de infección de las vías respiratorias superiores.
Conclusión: Se encontró que los pacientes ambulatorios recibían un alto índice de recetas con antibióticos en un hospital distrital de Afganistán, el cual correspondió al doble del 30% que recomienda la OMS. No se observó un incumplimiento sistemático de las dosis recomendadas, pero es posible que se hayan prescrito recetas inapropiadas para determinados cuadros clínicos. Los resultados del presente estudio ponen de manifiesto que el conocimiento de los factores determinantes de la receta de antibióticos en un contexto específico representa la primera etapa en el fomento de las prácticas idóneas prescripción en estos entornos.

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