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Title: Assessment of antimicrobial use and prescribing practices among pediatric inpatients in Zimbabwe

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Abstract

This study aims to assess antimicrobial consumption in the pediatric department of a tertiary care public hospital in Zimbabwe.

Clinical records of pediatric inpatients admitted to Harare Central Hospital over a 3-week period were reviewed prospectively. Antimicrobial consumption was described as days of therapy per 100 inpatient days (DOT/100 PD). Adherence of antimicrobial drug prescriptions to the National Guidelines was also evaluated.

A total of 121 (93.1%) children were prescribed at least one antimicrobial out of 130 children admitted. The median age was 14 months (IQR: 3 – 48 months).

Overall antimicrobial consumption was 155.4 DOT / 100 PD (95% CI 146-165.2). The most frequently prescribed antimicrobials were benzylpenicillin, gentamicin and ceftriaxone. Prescriptions were adherent to national guidelines in 57.7% of children.

This study shows that there is high antimicrobial drug usage in hospitalized children in Zimbabwe and a considerable proportion of prescriptions are non-adherent with national guidelines.

Introduction

Antimicrobial resistance (AMR) threatens our ability to effectively treat bacterial infections and leading to higher morbidity, mortality and costs.[1] One of the major drivers of AMR is inappropriate antimicrobial use.[1] In pediatric care, antimicrobials are among the most frequently prescribed medications. However, data on antimicrobial consumption in low-income settings are limited. Such data are crucially important to inform national action plans and antimicrobial stewardship programmes (ASPs).

This study aims to assess antimicrobial consumption in the pediatric department of a tertiary care public hospitals in Zimbabwe as a starting point for improving prescribing in this patient population.

Patients and methods

Harare Central Hospital (HCH) is one of two public-sector general hospitals in Harare, Zimbabwe, with a catchment population of 1 million, mainly from low-income communities. The hospital also receives referrals of seriously ill patients from other parts of the country.

Clinical records of pediatric inpatients admitted to two general pediatric wards at HCH over a 3-week period (26.06.2018-17.07.2018) were reviewed prospectively on a daily basis by a researcher who was not involved in prescribing. Patients were followed during the course of their admission. Patient characteristics, prescribed antimicrobials and their indication were recorded. Antimicrobial consumption was described as days of therapy per 100 inpatient days (DOT/100 PD)[2] with each antimicrobial contributing individually to the days of therapy. In addition, utilization patterns were analyzed according to age group. Prescribing was assessed against current Zimbabwe guidelines[3].

Following piloting, data were collected and entered into an electronic database using Open Data Kit (ODK 2.0, www.opendatakit.org). Data were analyzed using Stata/IC version 15 (Stata-Corp, TX, USA). Medians, interquartile ranges and proportions were calculated.

The study was approved by the Ethics Committees of HCH, the Medical Research Council of Zimbabwe (MRCZ/A/2255) and the London School of Hygiene and Tropical Medicine (ref. 15306).

Results

Over the study period, 130 children were admitted to the two medical wards. The median duration of hospital stay was 5 days (interquartile range (IQR): 3 – 7 days). More than half of the patients were boys, (80/130, 61.5%); median age was 14 months (IQR: 3 – 48 months); 13 (10%) were neonates, 42 (32.3%) infants, 46 (35.4%) children aged 1-5 years and 29 (22.3%) older children (≥5 years). Seven (5.4%) children were diagnosed with tuberculosis and 7 (5.4%) were HIV-infected. Four children died during the admission. The duration of follow-up ranged from one to fifteen days.

A total of 121 (93.1%) children were prescribed at least one antimicrobial. The total number of individual antimicrobials prescribed was 264. In 14 (11.6%) children, prescriptions were issued in the emergency department and immediately changed once the child was admitted to the ward. Antimicrobials were prescribed for the following most frequent clinical diagnoses: pneumonia (n=48, 39.7%), acute gastroenteritis (n=14, 11.6%), severe acute malnutrition (n=13, 10.7%), neonatal sepsis (n=12, 9.2%) and meningitis (n=7, 5.8%). The initial diagnosis was changed in 9/130 (6.9%) children.

When considering antimicrobials that were prescribed for at least 24 hours, the median number of antimicrobials prescribed was 2 (range 14), with 101 (84%) of the pediatric population receiving combination therapy. Most children (n=113, 93.4%) received intravenous antimicrobials.

The total number of inpatient days was 659 and a total 1024 DOT were prescribed (Table 1). Overall antimicrobial consumption was 155.4 DOT / 100 PD (95% CI 146-165.2). The DOT/ 100 PD according to the different age groups were 157.4 (95%CI 125.7-194.7), 161 (145.4-

177.8), 167.8 (95%CI 151.4-185.6) and 124.1 (95%CI 106.1-144.2) in neonates, infants, children aged 1-5 years and ≥5 years respectively. The most frequently prescribed antimicrobials were benzylpenicillin (n=68, 56.2%; 279 DOT), gentamicin (n=63, 52.1%; 253 DOT) and ceftriaxone (n=60, 49.6%; 281 DOT). Prescribed antimicrobials varied by age group: benzylpenicillin was the most commonly prescribed antimicrobial in infants (n=39; 72.2%) while older children were mostly prescribed ceftriaxone (n=21; 91.3%).

Out of the 121 children receiving antimicrobials, adherence to guidelines could be evaluated in 111. Among those, 64 (57.7%) received antimicrobials according to national guidelines. Prescriptions were adherent to national guidelines in 11/13 (84.6%), 36/47 (76.6%), 5/14 (35.7%) and 4/11 (33.3%) children diagnosed with severe acute malnutrition, pneumonia, acute gastroenteritis and neonatal sepsis. In children admitted with neonatal sepsis, non-adherence (n=7/11, 64%) was mostly due to the prescribing of ceftriaxone or benzylpenicillin and gentamicin for late onset neonatal sepsis whilst the guidelines recommend cloxacillin and gentamicin. For acute gastroenteritis, most cases (n=8/14, 57%) of non-adherence were due to the concurrent administration of ceftriaxone and ciprofloxacin. Stratified by age, prescriptions were adherent with guidelines in 6 (50%) neonates, 26 (65%) infants, 26 (61.9%) children 1-5 years old, and 6 (35.3%) children ≥5 years.

Discussion

We believe this is the first study to assess antimicrobial prescribing in pediatric inpatients in Zimbabwe as the country seeks to develop and implement its national action plan for combating AMR.[4] The majority of children admitted to the general pediatric ward at HCH received antimicrobials leading to high antimicrobial usage of 155.4 DOT/ 100 PD.

Antimicrobial usage was considerably higher than that seen in hospitalized children in high-income countries where rates varied from 29 DOT/100 PD to 94 DOT/100 PD)[2] and in other settings from Sub-Saharan Africa (114 and 67 DOT/100PD in South Africa and the Gambia,

respectively).[5, 6] The higher antimicrobial usage in this study may be explained by an overall higher proportion of children being prescribed antimicrobials (93% vs 54% in the Gambia), by the inclusion of neonates, and more frequent prescription of antimicrobial combinations. This may also reflect the high burden of infectious diseases in this setting, and the limited diagnostics available to confirm or refute bacterial infections leading to a syndromic management approach.

In this study, 93% of children admitted to hospital were prescribed at least one antimicrobial, which is comparable to data reported from South Africa, Ethiopia and Mozambique.[6-8] However, this is much higher than in Europe, where around 40% of children were on antimicrobials, perhaps due to high underlying infectious disease burden in Zimbabwe, increased supervision by senior pediatricians and better diagnostic capacity in high-income settings.[9, 10] A high proportion (84%) of children in our study received combination therapy accounting for the high DOT/100 PD.

Antimicrobial prescriptions adhered to national guidelines in 57.7% of cases, which is, slightly lower than in a referral hospital in Namibia (62%).[11] This may be due to the very rapid turn-over of the junior doctors who are the frontline for admitting children from the emergency department, and senior supervision may frequently be overstretched and unable to give sufficient oversight where there is diagnostic uncertainty. The relatively high number of prescriptions in discordance with national guidelines in our study may also be explained by limited access to microbiology diagnostics resulting in reduced confidence in diagnoses. Lack of AMR surveillance may lead to the prescribing of broader spectrum antimicrobials (using a "just in case" strategy). This was reflected in the relatively high usage of ceftriaxone (42.6 DOT/100PD) for a broad range of indications versus the more narrow range of indications recommended in the national guidelines.[3] The absence of institutional policies on rational antimicrobial use together with insufficient knowledge and training on antimicrobial prescribing, and unavailability of guidelines at the point of care, may also explain the high

frequency of antimicrobial prescriptions, combination therapies with overlapping spectrum (such as ceftriaxone and ciprofloxacin) and non-adherence.

This study is limited by the use of hospital records for recording prescriptions and diagnoses, making the findings dependent on the quality of documentation. Secondly, only two wards from a single hospital were evaluated over a 3-week period. However, the study was conducted in large referral hospital with high numbers of pediatric admissions and used a prospective follow-up strategy to ensure that all documented prescriptions are recorded. Also, any IV to oral switching of antimicrobials was not assessed. Overall though, we believe these findings are robust and represent the current standard of antimicrobial use among pediatric inpatients in Zimbabwe.

In conclusion, this study shows that there is high antimicrobial drug usage in children at the level of a referral hospital in Zimbabwe. However, a considerable proportion of prescriptions are non-adherent with national guidelines which is perhaps not surprising given the lack of monitoring and ASPs within the hospital. These findings emphasize the need for effective ASPs in Zimbabwe and for strengthening diagnostic capacity in low-income settings.

Disclosure of interest

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There are no conflicts of interest to declare

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