Prescribing Pattern and Antibiotic Use for Hospitalized Children in a Northern Nigerian Teaching Hospital

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Abstract

Background: Assessment of patterns of drug to detect performance problems and compliance with standards facilitates objective comparisons and impact evaluation. Children are at higher risk of consequences of irrational prescribing and antibiotic misuse. Objective: The objective of the study was to evaluate the prescribing pattern and utilization of antibiotics for children using standard prescribing indicators and indices of rational drug prescribing. Materials and Methods: This was a retrospective study of prescriptions for pediatric inpatients at a teaching hospital in Northern Nigeria. Information was obtained from eligible prescriptions received over 24-month period using a modified WHO prescribing indicator form. The WHO prescribing indicators and the Index of Rational Drug Prescribing (IRDP) were used to evaluate prescriptions. Data were analyzed and presented as proportions, means, tables, and charts, comparing with WHO standards and with findings of similar studies. Results: There were 3908 eligible prescription orders, with a mean patient age of 3.1 (±2.7) years. With an average of 2.1 drugs per prescription, 66.8% were written with generic names, whereas a single antibiotic was included among 63% of prescriptions with antibiotics. Antibiotics and injections were contained in 49.5% and 67.7% of prescriptions, respectively. Medications were available in the Essential Medicines List in 95.5% of cases. The IRDP obtained is 2.99, against a standard of 5. Aminoglycosides, cephalosporins, and penicillins were the most common choices, whereas ampicillin/cloxacillin was the most common combination. Conclusion: Drug prescribing and antibiotic use were generally inappropriate compared with ideal standards. Continuous training/retraining on rational drug use, periodic monitoring, and use of treatment protocols in tertiary hospitals are recommended.

Keywords: Antibiotic children, essential medicines, irrational drug use, Nigeria, prescriptions, teaching hospital

Résumé

Contexte: L’évaluation des tendances de la consommation de drogues pour détecter les problèmes de performance et de la conformité aux normes facilite la comparaison objective et l’évaluation de l’impact. Les enfants sont plus à risque de conséquences d’abus d’antibiotiques de prescription et d’irrationnel. Objectif: L’objectif de l’étude était d’évaluer la tendance de la prescription et l’utilisation des antibiotiques pour les enfants à l’aide de norme prescrivant d’indicateurs et d’indices de la prescription rationnelle des médicaments. Matériels et méthodes: Il s’agissait d’une étude rétrospective d’ordonnances pour les patients pédiatriques d’un hôpital d’enseignement dans le nord du Nigéria. L’information a été obtenue à partir d’ordonnances admissibles ont reçu plus de 24 mois à l’aide d’une prescription qui modifiée sous forme d’indicateurs. Les indicateurs de prescription qui et l’indice de la prescription rationnelle des médicaments (PDIR) ont été utilisés pour évaluer les prescriptions. Les données ont été analysées et présentées en tant que proportions, signifie, tableaux et graphiques, la comparaison avec les normes de l’OMS et des constatations d’études semblables. Résultats: Il y avait 3908 ordonnances ordonnance admissibles, avec une moyenne d’âge du patient, de 3,1 (± 2,7) ans. Avec une moyenne de 2,1 médicaments par ordonnance, 66,8 % ont été écrits avec des noms génériques, alors qu’un seul antibiotique a été inclus parmi les 63% des ordonnances avec des antibiotiques. Les antibiotiques et les injections ont été contenues dans 49,5% et 67,7% des ordonnances, respectivement. Médicaments étaient disponibles dans la liste des médicaments essentiels dans 95,5% des cas. Le PDIR obtenu est

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Introduction

Irrational prescribing, polypharmacy, use of “off-label,” drugs and medicines with improper efficacy are common in developing countries.[1-3] Inappropriate antibiotic use, overuse of injections, and erroneous prescription writing have been identified as the most common forms of irrational use of medicines worldwide.[4-6] The magnitude of irrational drug use is enormous in developing countries where high burden of infections, limited antibiotic availability, and poor regulation of drug use coexist.[4,6] In spite of being an issue of public health concern, regulations to curtail the trend have remained largely inadequate.[7] The advent of antibiotic therapy later became accompanied by dire consequences of their misuse including emergence and spread of drug-resistant pathogens, escalating costs of care with increased morbidity and mortality.[1,8-10] It has been estimated that between 20% and 50% of all antibiotic use is inappropriate.[9] Currently, Nigeria has a National Drug Policy that addresses rational prescribing, but the policy lacks specific regulations on antibiotic use.[11]

Medication errors are any failure in the treatment process that leads to or has the potential to lead to harm to the patient and include mistakes of prescribing, administering, dosing, and duplication.[9] Prescription errors are any failure in prescription writing process that results in wrong instructions about the normal features of a prescription.[9] These features include the identities of the recipient, the prescriber and that of the medicine, dosage, formulation, route, timing, frequency, and duration of administration.[9,12] Prescribing errors have been reported in all age groups across the world, raising concerns on medication safety, especially among vulnerable groups.[13] Children are more at risk of the adverse effects of medication errors due to unique peculiarities of body size, surface area, drug metabolism, and excretion.[14] Several studies have shown that dosing errors are consistently the most prevalent forms of medication errors among prescriptions for children and adjustments based on the unique peculiarities of children helps prevent these errors.[15,16]

Among studies on inpatient pediatric prescriptions in developing countries, Deshmukh and Mahajan et al., in India, observed 79% of prescriptions containing two antibiotics with 96% being parenteral forms whereas 48.92% were written in generic name.[17] Cole et al., in Sierra Leone, reported 82.99% of prescriptions containing antibiotics, being also the second most commonly prescribed medicines.[18] In Nigeria, Anyanwu and Arigbe-Osula[19] found between 63.3% and 86.6% of prescriptions containing antibiotics, whereas the rate of antibiotic prescribing was higher for children aged 1–5 years compared to other groups combined. They also found that 80%–86% of antibiotics were parenteral and 80%–85.5% were prescribed from the hospital formulary with the most common being cephalosporins, penicillin, and aminoglycosides.[19]

Irrational prescribing may lead to ineffective and/or harmful treatment, elongation of duration of illness, and increased costs.[20-23] Major determinants of prescribing habits include influence of mentors and pharmaceutical sales representatives and patient peculiarities.[24-26] In teaching hospitals, trainees often exhibit prescribing habits reflecting the influence of senior colleagues, whom they consistently emulate in a didactic tradition.[26]

The WHO prescribing indicators and the Index of Rational Drug Prescribing (IRDP) are recognized as the basic minimal standard for promoting rational drug use, monitoring, and evaluation of drug utilization.[27-29] Most studies from tertiary hospitals in Nigeria reported on prescriptions for adult outpatients, leaving a gap of information for pediatric inpatients. A literature search using PubMed, MEDLINE, HINARI, Google Scholar, and Africa Journals Online, with appropriate search terms revealed only a few studies on outpatients that assessed prescribing using the WHO indicators[30-32] Although developed for use in outpatient settings in primary level facilities, the indicators have also been applied for inpatient settings of tertiary hospitals.[5,6,17,18,30-32]

The aim of this study was to investigate prescribing and antibiotic use, employing the WHO core indicators.

Materials and Methods

Study center

The study center is a training and referral center with over 800-bed capacity that provides health-care services for many states across Northern Nigeria. The facility has a pediatrics department with admission units including the emergency pediatric unit (EPU), a special care baby unit, pediatric medical ward, and the pediatric surgical ward. Patients are referred for admission from the delivery suite, the general outpatient department, and the accidents/emergency units as well as the weekly subspecialty clinics. There has neither been any drug monitoring activity nor antibiotic stewardship program conducted in the hospital before and during the study period.

Study design

The study was of a descriptive retrospective design involving
inpatient prescription orders of children that were on admission, received at the main hospital pharmacy over the 24-month period from January 1, 2013 to December 31, 2014.

**Study sample**

All eligible prescription orders for children below the age of 18 years that were on admission within the study period were included and constituted the study sample. The WHO recommends sample size of a minimum of 600 encounters as the ideal for retrospective evaluation of prescriptions that should be obtained through random sampling. However, the consideration for potential effects of seasonality of illness presentations and fluctuations in patronage of hospital services due to other reasons in this study informed the decision to include all eligible prescriptions within the study period, even though a less preferred method as suggested by the WHO.

**Exclusion criteria**

Prescription orders that were not legibly written and considered not readable were not included, as well as those containing only intravenous infusions, consumable items, and vaccines. Any prescriptions without relevant client identity (age, registration number, and ward address) were excluded from the study. Prescriptions that were repeated with the same drugs and those revised were also excluded from the study.

**Data collection**

Information collected from the prescription order forms include compliance with standard prescription format and specific indicators including age, sex, registration number, body weight, prescriber (doctor’s) name, and signature. Others include names of medicines prescribed, dose, route, strength, frequency and instructions for medication use, number of drugs prescribed, and duration of treatment. Dosage and frequency of administration of antibiotics were also compared with standard in the BNF and the EMDEX Paediatric Drug Guide 2013 (based on WHO Model Essential Medicines List [EML] for Children).

Trained Intern Pharmacists extracted relevant data and entered these into a standardized prescribing indicator form as adapted from the WHO.

**Data analysis**

The prescriptions were evaluated in conformity with the methods of deriving core prescribing indicators recommended by the WHO. This includes the average number of drugs contained per encounter (drugs prescribed divided by total number of eligible encounters), number of drugs prescribed using generic names divided by total number of drugs prescribed, multiplied by 100 (percentage), and number of prescriptions with an antibiotic prescribed divided by total number of eligible encounters multiplied by 100 (percentage). Others are the number of prescriptions, in which an injection was prescribed divided by a total number of eligible prescriptions, multiplied by 100 (percentage) and the number of drugs prescribed from the EML (Essential Drug List [EDL]) divided by total number of drugs prescribed, multiplied by 100 (percentage).

To further explore the extent to which the prescriptions met the ideal standards of rational drug prescribing, the five respective WHO core indicators were used to derive the IRDP. We adopted a validated method of indexing, which was also used in a similar report on prescribing pattern for children in India by Atif et al. and in Sierra Leone by Cole et al. It consists of scores derived from the five components of the WHO prescribing indicators. The ideal or optimal level for each indicator is shown Table 1. The WHO prescribing indicators were allotted an optimal index score of one such that calculated indices closer to one were considered as more rational prescribing. The polypharmacy index was calculated from the percentage of nonpolypharmacy prescriptions, with prescriptions containing less than four drugs considered as nonpolypharmacy. Generic name and essential drug indices were obtained from the percentage of drugs prescribed by generic name and from the EDL, respectively. The index of rational antibiotic prescribing was obtained by dividing the optimal level (30%) by the percentage of prescriptions containing antibiotic(s). The index of injection use was calculated by dividing the optimal level (10%) by the percentage of prescriptions containing injectable drugs.

The IRDP, which has an optimal maximum value of five as shown in Table 1, was then calculated by adding the five corresponding indices obtained from the results.

Computer data entry was carried out into Excel spreadsheet and data analysis was carried out using SPSS version 20 (IBM, Corp., Armonk, NY, USA); results were presented as frequencies and proportions, contingency tables, and charts. Means and percentages were also calculated.

**Ethical considerations**

Ethical approval was obtained from the facility Institutional Ethics Review Board before commencement of the study.

**RESULTS**

**Demographic features**

A total of 3924 prescription orders for children who were managed in the various admission wards within the study period were received at the main hospital pharmacy during the study period, of which 16 that were considered not eligible were excluded from the study. Among the 3908 eligible prescription orders, 60.6% were for males and 32.8% were for infants and 32.6% for toddlers and preschool children aged up to 5 years, with a mean age of 3 years 13 months. The highest proportion of prescriptions was for children seen at the EPU (40.1%) (Table 2).

**Prescription writing formats**

Majority of the prescriptions had complete patient biodata written (99.8%), while only 40.3% and 87.4% had names and signatures of the prescribers, respectively [Figure 1]. There were 29.6% of prescriptions that contained just one drug whereas 25.4% contained two drugs and the proportion of prescriptions with 4 or ≥5 drugs were 14.2% and 9.3%, respectively [Figure 2].
Core prescribing indicators and index of rational drug prescribing

Table 3 gives a summary of these indicators side by side with previously derived values obtained from studies in Nigeria, compared with the WHO/IRDP standards. While the mean number of drugs per prescription was 2.1, majority (95.5%) of drugs available in the prescription orders were available in the facility EDL. Use of generic names in the prescriptions was observed in 66.6%, whereas 49.5% of encounters contained one or more antibiotics. Encounters that had injectable drugs constituted 67.7%.

The IRDP as obtained from the component indices in this study was 2.99. Injection and antibiotic prescribing had the lowest scores (0.15 and 0.44, respectively) while essential drug index had the highest index score (0.96). Table 4 summarizes the IRDP obtained for all the inpatient prescriptions studied, alongside the ideal standard.

![Figure 1: Compliance with standard prescription writing format](image1)

![Figure 2: Number of drugs per prescription](image2)

### Table 1: Optimal scores of prescribing indicators

| WHO prescribing indicators (%) | Optimal level (%) | Optimal index score |
|--------------------------------|------------------|-------------------|
| Nonpolypharmacy prescriptions | ≤3               | 1                 |
| Drugs prescribed by generic names | 100             | 1                 |
| Prescriptions with antibiotics | ≤30              | 1                 |
| Prescriptions with injections | ≤10              | 1                 |
| Drugs prescribed from the EDL | 100              | 1                 |

EDL=Essential drug list

### Table 2: Demographic characteristics of children with eligible prescriptions

| Parameter                        | n (%) |
|----------------------------------|-------|
| Age (years)                      |       |
| <1                               | 1283 (32.8) |
| 1-5                              | 1271 (32.6) |
| >5-10                            | 920 (23.5) |
| >10                              | 434 (11.1) |
| Sex                              |       |
| Female                           | 1531 (39.2) |
| Male                             | 2369 (60.6) |
| Not indicated                    | 8 (0.2) |
| Source of prescription orders    |       |
| EPU                              | 1568 (40.1) |
| SCBU                             | 693 (17.8) |
| PSW                              | 646 (16.5) |
| PMW                              | 1001 (25.6) |
| Total                            | 3908 (100) |

EPU=Emergency paediatric unit, SCBU=Special care baby unit, PSW=Paediatric surgical ward, PMW=Paediatric medical ward

### Table 3: The WHO core prescribing indicators assessed for drug prescriptions

| Prescribing indicators | Encounters | Average/percentage | Previously derived in Nigeria | WHO standard derived or ideal |
|------------------------|------------|-------------------|-------------------------------|------------------------------|
| Drugs per encounter    | 3908 (total)| 2.1 (average)     | 3.8                           | 1.6-1.8                      |
| Percentage of drugs prescribed with generic name | 2609 | 66.6% | 58% | 100% |
| Encounters with any antibiotic (s) prescribed | 1933 | 49.5% | 48% | 20%-20.6% |
| Encounters with injections | 2464 | 67.7% | 37% | 13.4%-24.1% |
| Percentage on EML*     | 3732       | 95.5%             | NA                            | 100%                         |

*EML=Essential medicines list

### Table 4: Calculated indices of rational drug prescribing

| Polypharmacy | Generic prescribing | Rational antibiotic prescribing | Rational injection prescribing | Essential drug index | IRDP* (total) | Ideal IRDP* |
|--------------|---------------------|---------------------------------|-------------------------------|----------------------|--------------|-------------|
| 0.77         | 0.67                | 0.44                            | 0.15                          | 0.96                 | 2.99         | 5.0         |

*IRDP=Index of rational drug prescribing
Antibiotic prescriptions

Among the prescription orders containing antibiotics, the average number of antibiotics per encounter was 2.3. Whereas a majority of antibiotic-containing prescription orders had optimum dosages (74.6%) of antibiotics [Figure 1], up to 20.4% and 5% of the prescribed antibiotics were underdose and overdose, respectively. The majority of inpatient prescriptions had a single antibiotic (63%), whereas 3.2% and 0.7% had three or more antibiotics, respectively, as shown in Table 5, whereas the leading combination of antibiotics prescribed as shown in Table 6 reveals that β-lactam combinations alone or with gentamicin were the three leading combinations prescribed. Figure 3 shows the major classes of antibiotics prescribed for children admitted to the ward facilities. Aminoglycosides (particularly gentamicin) were the most common, followed closely by cephalosporins and β-lactam penicillins, whereas the most frequent combination antibiotics were ampicillin-cloxacillin (38.1%).

**Figure 3: Most frequently prescribed classes of antibiotics (either as single or in a combination)**

**Discussion**

This study found a high rate of antibiotic use for children, the majority of who were aged 5 years and below, being also predominantly male with about three-quarter admitted in the medical wards. The predominance of the younger age group could be a reflection of the larger infectious disease burden among under-five children,[17] warranting the use of antibiotics. There was also a male preponderance found, which has similarly been observed in previous reports of studies on prescriptions for children admitted in hospitals in Sierra Leone, India, and Ethiopia.[17,18,35,36,38,39] It is not clear in our study, the reason for male predominance in the population of children that received prescriptions over the period studied, but male child preference (and selective priority in care for children) as suggested in those studies from India,[35,36,38,39] may also be the reason in the communities served by the facility studied.

The finding of almost a quarter of all prescription orders that contained four or five drugs, suggest a tendency for polypharmacy in the prescribing habits that prevailed in the facility. Furthermore, an average of 2.1 drugs prescribed per patient encounter, being higher than the WHO recommended standard range of 1.6–1.8,[27] is further evidence of that tendency for polypharmacy. The value is, however, much lower than a previously derived finding (3.8) from an earlier study (involving Nigeria) that also established the recommended average for developing countries.[27] Although the WHO standard value was obtained largely from adult outpatient settings across developing countries (with fewer pediatric prescriptions),[27] they remain the only valid reference standards available for such comparison. Compared to what was reported in similar studies in Ethiopia, Sierra Leone, Nigeria, and India,[5,6,17-19,30-32] the average of 2.1 drugs per encounter in this study is the lowest even though just slightly above the WHO standard. The difference between the finding in this study and these cited reports could, however, be attributed to differences in study methodology. The use of inpatient treatment chart reviews in some of these studies,[17,19,30-32] perhaps did allow for obtaining the total number of drugs used per patient over the period of their admission, which will tend to give higher average number of drugs than what was obtained with only prescription orders in this study. Polypharmacy could potentially predispose to higher risk of drug–drug interactions and other adverse events.[11,14,15] Similarly, redundant medicines within a prescription and use of brand names can add to the financial burden on patients and health-care resources.[3,11,12]

The use of generic names in prescription writing, even though an obvious practice found in up to two-thirds of prescriptions analyzed, is still much lower than the WHO standard of 100%. This finding implies that there is a high rate of use of brand names in prescription writing among
practitioners in this facility. It may suggest an undue influence of mentors’ prescribing habits or that of pharmaceutical sales representatives (as alternative source of drug information available to prescribers). It does also suggest a less than optimal utilization of treatment protocols and the facility EML. In a study of the factors influencing prescribing habits, Oshikoya et al. reported that prescribers mentioned the influence of pharmaceutical sales representatives on their prescribing practices and use of trade names. Generic prescribing has been identified to be much simpler, facilitates communication and clarity between health-care providers and clients, as well as being relatively cheaper than medicines prescribed with brand names. Nevertheless, the proportion of prescriptions with generic names in this study is less than the 71% reported in Sierra Leone, and much higher than the 48.9% reported from India. The relatively higher generic prescribing index obtained in this study could be explained by a relatively better level of compliance by prescribers in using the facility EML compared to the report from India. It is noteworthy that a great majority of the drugs prescribed were obtained from the facility EML, which implies that the stock list is robust enough to provide for the needs of most patients. It has been suggested that implementing interventions to monitor and ensure drug prescribing from the EML, which mostly comprises generics, could mitigate trends in nongeneric prescriptions. This is especially because EMLs are selected from a public health perspective to address priority health-care needs of the population, ensuring efficacy, safety, and comparative cost-effectiveness.

Although the majority of antibiotic prescriptions were found to be accurate in dosage per unit body weight (Kg), significant proportions had doses outside the recommended ranges as provided in both the 2010–2011 British National Formulary for children and the 2013 Emdex Paediatric Drug Guide used in Nigeria. Use of higher doses has implications for safety, with a tendency to cause dose-dependent side effects and adverse drug reactions. Conversely, use of insufficient doses than the recommended could lead to the development of bacterial resistance, poor therapeutic response, and treatment failure. These may also ultimately lead to decision to change antibiotics, thereby adding more costs and prolongation of treatment.

A proportion of close to one-half of all prescription orders containing antibiotics in this study is suggestive of evidence of unnecessary antibiotic use, being over twice as much as the WHO recommended standard. Anyanwu and Arigbe-Osula reported the presence of antibiotics in up to 63.3%–86.6% of inpatient prescriptions of admitted children in a tertiary hospital in southeastern Nigeria, whereas Cole et al., also reported up to 74.8% of prescriptions containing antibiotics. It could be reasonable to presume that children (especially under-fives) in this study could have received more antibiotics in their prescriptions as a consequence of their vulnerability to infectious disease, which has been recognized in the global epidemiology of child morbidity and mortality.

The smaller proportions of prescriptions containing three or more antibiotics may be partly a reflection of the tendency for polypharmacy discussed earlier. However, the presence of combination drug regimens for tuberculosis or multiple antibacterial agents could also have contributed to these prescriptions with three or more antibiotics.

The rate of injection use is above thrice the WHO recommended and about twice the previously obtained value in Nigeria. The tendency for use of more injections than the ideal is evidence for irrational medicines’ use of a public health concern. Apart from its potential to generate hazardous waste, it predisposes to unwarranted pain, promotes the spread of blood-borne infections, development of complications, and promotes microbial resistance. Irrational prescribing of antibiotics and injections increases health-care costs and adds extra strain on the already weak health infrastructure and human resources. In this study, injections were prescribed more than necessary, with 67.7% (IRDP of 0.15) of all prescriptions having at least one injection. Anyanwu and Arigbe-Osula also reported 80%–86% of drugs administered parenterally among pediatric inpatients in a tertiary hospital, with 80%–85.5% of drugs prescribed from the hospital formulary. Comparatively lower injection prescribing rates of 20% were noted in a similar study among admitted children in Sierra Leone, but the rate was up to 96% in Pakistan.

Whereas our finding of the three leading classes of antibiotics prescribed (gentamicin, cephalosporins, and β-Lactam penicillins) appeared similar with those of Anyanwu and Arigbe-Osula, the order of the most common antibiotics was reversed, with cephalosporins, β-Lactam penicillins followed by aminoglycosides, as the three most frequently prescribed antibiotic classes in that study.

Some of the limitations in this study include being purely a descriptive study design. As such, no qualitative component in the methods to determine appropriateness of and underlying factors that influence prescribing, especially for antibiotics and those for trends toward polypharmacy and selective use of parenteral route of administration. There was also no information analyzed for appropriateness of prescribed medications for specific diagnoses, nor laboratory evaluation to justify therapeutic choices of prescribed drugs. Further studies are, therefore, needed to address these gaps.

**Conclusion**

This study provides baseline information on rational prescribing for children admitted to a teaching hospital, upon which objective comparison could be made with future assessments as part of interventions to monitor and evaluate prescribing practices. The findings reveal evidence of inappropriate prescribing practices, which have potential implications of being passed on as a function of mentorship, teaching, and instructions by senior cadre of staff to medical trainees at various levels. There is, therefore, a pressing need for introduction of antibiotic stewardship programs, with
reorientation on evidence-based rational use of medicines for all cadres of physicians in Nigerian teaching hospitals. The need for curriculum review to include comprehensive instruction on the rational use of medicines for undergraduates cannot be overemphasized.

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Conflicts of interest

There are no conflicts of interest.

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