Drug prescribing and potential drug-drug interactions at the paediatric unit of a secondary health facility in Southern-Ijaw Local Government Area, Niger Delta Region, Nigeria

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ABSTRACT

Background: Drug interactions resulting from multidrug prescribing can be desirable and/or non-desirable.

Objectives: To assess drug prescribing and potential drug-drug interactions at the paediatric unit of Amassoma General Hospital in the Southern-Ijaw Local Government Area, Bayelsa State, Niger Delta Area of Nigeria.

Methods: Retrospective evaluation of randomly selected 227 case notes of paediatric patients (aged, ≤12 years), who attended clinics at the study center from January 01 to December 31, 2020 was carried out. Pertinent data collected on diseases, medications prescribed, selected prescribing indicators, and potential drug-drug interactions (pDDIs) identified were presented descriptively, in simple percentages, mean, and median as appropriate. Where necessary, average values were compared using student-t test, and a p-value less than 0.05 was considered statistically significant.

Results: Each of the paediatric patients presented with average of 2.07 ± 0.79 diseases per encounter, and majority (252, 56.2%) were treated for infections. Average of 4.37 ± 1.73 drugs were ordered per encounter, and anti-infectives (423, 42.8%) were the most prescribed. All selected prescribing indicators were not within referenced standards, excluding encounters with injections prescribed (19.2%). A total of 160 (70.5%) of all 227 prescriptions vetted contained at least a pDDI. In all, average of 1.35 ± 1.28 pDDIs were observed per prescription, of which 0.93 ± 0.82 and 0.42 ± 0.77 (p < 0.05) were desirable and non-desirable, respectively. Adverse events (72, 74.2%) and reduction in effectiveness (25, 25.8%) of medication therapy constituted the main potential clinical consequences of non-desirable pDDIs identified.

Conclusion: The paediatric patients seen at the study center routinely present with infections, and were mostly prescribed anti-infective agents. Drug prescribing practice observed was grossly suboptimal and there were several cases of non-desirable pDDIs.

Keywords: Bayelsa State, Drug Prescribing, Niger Delta Area, Potential Drug-drug Interaction, Paediatric Patients, Southern Ijaw Local Government Area

Prescription de médicaments et interactions médicamenteuses potentielles à l'unité pédiatrique d'un établissement de santé secondaire dans la zone de gouvernement local de Southernijaw, région du delta du Niger, Nigéria

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RÉSUMÉ

Contexte : Les interactions médicamenteuses résultant de la prescription de plusieurs médicaments peuvent être désirables et/ou indésirables.

Objectifs : Évaluer la prescription de médicaments et les interactions médicamenteuses potentielles à l'unité pédiatrique de l'hôpital général d'Amassoma dans la zone de gouvernement local de Southern-Ijaw, État de Bayelsa, région du delta du Niger au Nigeria.

Méthodes : Une évaluation rétrospective de 227 notes de cas de patients pédiatriques (âgés de ? 12 ans) sélectionnés au hasard, qui ont fréquenté les cliniques du centre d'étude du 1er janvier au 31 décembre 2020 a été réalisée. Les données pertinentes recueillies sur les maladies, les médicaments prescrits, les indicateurs de prescription sélectionnés et les interactions médicamenteuses potentielles (IMP) identifiées ont été présentées de manière descriptive, en pourcentages simple, moyenne et médiane, selon le cas. Si nécessaire, les valeurs moyennes ont été comparées à l'aide du test t de Student, et une valeur de p inférieure à 0,05 a été considérée comme statistiquement significative.

Résultats : Chacun des patients pédiatriques a présenté en moyenne 2,07 ± 0,79 maladies par consultation, et la majorité (252 soit 56,2 %) ont été traités pour des infections. Une moyenne de 4,37 ± 1,73 médicaments ont été prescrits par consultation, et les anti-infectieux (423 soit 42,8 %) étaient les plus prescrits. Tous les indicateurs de prescription sélectionnés n'étaient pas conformes aux normes de référence, à l'exception des rencontres avec des injections prescrites (19,2 %). Au total, 160 (70,5 %) des 227 ordonnances approuvées contenaient au moins un IMP. Au total, une moyenne de 1,35 ± 1,28 IMP a été observée par prescription, dont 0,93 ± 0,82 et 0,42 ± 0,77 (p < 0,05) étaient respectivement désirables et non désirables. Les effets indésirables (72, 74,2 %) et la réduction de l'efficacité (25 soit 25,8 %) de la thérapie médicamenteuse constituaient les principales conséquences cliniques potentielles des IMP indésirables identifiées.

Conclusion : Les patients pédiatriques vus au centre d'étude présentaient régulièrement des infections et se voyaient pour la plupart prescrire des agents anti-infectieux. La pratique de prescription de médicaments observée était nettement sous-optimale et il y avait plusieurs cas de IMP indésirables.

Mots-clés : État de Bayelsa, prescription de médicaments, région du delta du Niger, interaction médicamenteuse potentielle, patients pédiatriques, région du gouvernement local de Southern Ijaw.

INTRODUCTION

The need to ensure that patients are provided with appropriate medications that meet World Health Organization's (WHO) specifications has been noted as the main reason for which studies on drug utilization are conducted at various health facilities. Often times, many of these studies are designed to address medication use only in adult patients.[1,2] Meanwhile, just as it is for adults, paediatric patients also are routinely prescribed medications for the management of various forms of health conditions. These medications often range from prescription only to over-the-counter drugs. Importantly, a patient may present with certain condition(s) in which multidrug prescribing is required for effective therapy.[3] When multiple medications are prescribed, polypharmacy, with its attendant safety issues, especially those resulting from drug-drug interactions (DDIs) are often parts of many challenges to contend with.[2,3]

Most of the previous works done on impacts of DDIs on outcomes of therapy have largely ignored possibility of such interactions resulting in desirable clinical effects.[3,4] Instead, the focus has always been on negative impacts of DDIs. The foregoing is particularly more palpable in studies assessing the use of multiple medications in special populations, notably among elderly and paediatric patients. For the paediatric population, multidrug prescribing is discouraged where possible given their vulnerability to the danger posed by polypharmacy on efficacy of interacting medications and/or precipitation of adverse drug events.[3,5] Notwithstanding the issues raised above, some children presenting with certain health conditions or comorbidities will benefit from combination of medicines, provided this is done as therapeutically appropriate, while taking into consideration the need to weigh the risks of undesirable to the benefits of desirable clinical outcomes.[6]

Potential DDIs (pDDIs) and the consequent clinical outcomes resulting from multidrug prescribing have been exploited for the purpose of enhancing effectiveness of therapy in several health conditions of public health importance. For instance, patients suffering from conditions like human immunodeficiency virus (HIV) infection, malaria, diabetes mellitus, hypertension, tuberculosis, leprosy et cetera have been noted to benefit immensely from combination therapy.[7] The rationale for therapy in the foregoing is hinged on combining drugs with diverse mechanisms of actions/interactions that are beneficial to the concerned patient. Obviously, it is worthy to note that occurrence of drug interactions is inevitable in situations in which multiple drugs are prescribed, and that their negative impacts can be mitigated by adopting good prescribing practice.[7,8]

Paucity of information on drug utilization and DDIs among children in Bayelsa State in the Niger Delta Area of Nigeria necessitated the present study. Thus, this study was aimed at assessing drug prescribing practice and pDDIs at the paediatric unit of the Amassoma General Hospital, which is located in the Southern Ijaw Local Government Area of Bayelsa State, in the Niger Delta region of Nigeria.

METHODS

Study setting

The study was conducted at the paediatric unit of Amassoma General Hospital, which is a secondary health facility located in a semi-urban community in the Southern Ijaw Local Government Area of Bayelsa State, South-South, Nigeria. The hospital provides comprehensive healthcare services to the residents of Amassoma and its neighboring riverine communities. A total of 1,602 patients were seen at the health facility within the study period (year 2020). Five hundred and fifty-one (34.4%) of these were paediatric cases.

Study design

The study involved a descriptive, cross-sectional, retrospective evaluation of randomly selected 227 from a total of 551 case notes belonging to paediatric patients (aged, ≤ 12 years), who attended clinics at the paediatric unit of the study center from January 01 to December 31, 2020. The sample size was derived with the aid of the sample size calculator by Qualtrics XM (www.qualtrics.com) at Confidence Level of 95% and 5% margin of error. Case notes of all paediatric patients assessed were selected by means of systematic random sampling technique, while using the clinic attendance register as a guide.

Data collection procedure

Following ethical approval, appropriately structured data collection form was developed and used for the collection of the relevant patient's information. These included their demographics (mainly age and gender), status (whether managed as inpatient or outpatient), and diseases presented. Information on drugs prescribed were also collected and the prescribing practice by the prescribers at the study center assessed in relation to selected WHO prescribing indicators.[1,9] Diseases treated

and medications prescribed were classified in accordance with guidelines by the International Classification of Diseases 11th Revision (ICD-11)[10] and WHO Collaborating Centre for Drug Statistics Methodology,[11] respectively. The Epocrates® Application (www.epocrates.com) was employed as a guide for the identification of potential drug-drug interactions (pDDIs) among all medications prescribed for the children within the study period, and they were classified as either desirable or non-desirable. The non-desirable pDDIs were further categorized into those that may cause reduction in therapeutic activity and those that may precipitate adverse events in the patients. The adverse events categories were in turn disaggregated according to the organ-systems affected in the body.

Data analysis
Data collected were analyzed with the aid of Statistical Package for Social Sciences (SPSS) version 23 and GraphPad Instat 3.10 for Windows (GraphPad Software, San Diego California USA). Results generated were expressed in simple percentages and presented in tabular formats. Average values were presented in mean ± standard deviation (SD) and median (IQR = interquartile range) as appropriate. Average numbers of desirable and non-desirable pDDIs per encounter were compared using student-t test, and a p-value less than 0.05 was considered statistically significant.

RESULTS
More female (123, 54.2%) than male (104, 45.8%) paediatric patients, of whom most were infants (94, 41.4%) aged, 1 - 23 months were encountered within the study period. Their median age (month) was 36.0 (IQR = 60), and they were mostly treated as out-patients (131, 57.7%). These and other demographic characteristics are as presented in Table 1.

Table 1: Patients' characteristics (n = 227)

Characteristics of the paediatric patients	N (%)
Gender	
Male	104 (45.8)
Female	123 (54.2)
Age	
Neonate (≤ 30 days)	1 (0.4)
Infant (1 – 23 months)	94 (41.4)
Young child (2 – 5 years)	69 (30.4)
Child (6 – 12 years)	63 (27.8)
Status of patient	
In-patient	96 (42.3)
Out-patient	131 (57.7)

N, number of observations; n, Sample size; Median age (month) of the paediatrics, 36.0 (IQR = 60).

Most of the children seen presented with two diseases (99, 43.6%), and were followed by those who were diagnosed with one (67, 29.5%) and three diseases (61, 26.9%). Majority were treated for infectious or parasitic diseases (252, 56.2%). In addition, several others were diagnosed with diseases of the digestive system (78, 17.4%), the skin (40, 8.9%), the respiratory system (39, 8.7%), the blood or blood forming organs (12, 2.7%), and the musculoskeletal system or connective tissue (12, 2.7%), among others (Table 2).

Table 2: Diseases diagnosed among the paediatric patients

Disease variables	N (%)
Number of diseases diagnosed per patient (n = 227)	
One	67 (29.5)
Two	99 (43.6)
Three	61 (26.9)
Classes of Diseases diagnosed (n = 448)	
Certain infectious or parasitic diseases	252 (56.2)
Diseases of the digestive system	78 (17.4)
Diseases of the skin	40 (8.9)
Diseases of the respiratory system	39 (8.7)
Diseases of blood or blood forming organs	12 (2.7)
Diseases of the musculoskeletal system or connective tissue	12 (2.7)
Diseases of the nervous system	6 (1.3)
Diseases of the genitourinary system	4 (0.9)
Diseases of the visual system	2 (0.5)
Injury, poisoning or certain other consequences of external causes	2 (0.5)
Disease of ear or mastoid process	1 (0.2)

Mean ± SD; SD, standard deviation; Average number diseases diagnosed per patient, 2.07 ± 0.79

The patients treated in this study were mostly prescribed four (60, 26.4%) or more (96, 42.3%) medications. Meanwhile, those who received one (10, 4.4%) or two (20, 8.8%) drugs were in the minority. In treating conditions diagnosed, the duration for which a given medication therapy was mostly prescribed at average of 6.28 ± 1.97, was 5 or more days (195, 85.9%). The most employed means of medication administration were oral (781, 79.0%), distantly followed by parenteral (183, 18.5%) routes, while some medications were also prescribed for transdermal (22, 2.2%), ocular (2, 0.2%), and nasal routes (1, 0.1%) of administration. Of all 989 medications ordered for all cases evaluated, 423 (42.8), 197 (19.9), and 112 (11.3) were respectively prescribed as anti-infective drugs for systemic use, drugs working on the musculoskeletal system, and drugs working in the alimentary tract and metabolism. Some other 66 (6.7%), 54 (5.5%), 40 (4.0%), and 24 (2.4%) medications among others were prescribed as drugs working in the blood and blood forming organs, drugs working on the skin, drugs working on the respiratory system, and drugs working as antiparasitic products, insecticides and repellants, respectively (Table 3).

Table 3: Pattern of drug prescribing among the paediatric patients

Characteristics of drugs prescribed	N (%)
Number of drugs prescribed per patient, 1 – 9 drugs (n = 227)	
1 drug	10 (4.4)
2 drugs	20 (8.8)
3 drugs	41 (18.1)
4 drugs	60 (26.4)
= 5 drugs	96 (42.3)
Duration of drug therapy, 1 – 14 days (n = 227)	
1 day	4 (1.8)
2 days	6 (2.6)
3 days	18 (7.9)
4 days	4 (1.8)
= 5 days	195 (85.9)
Route of drug administration (n = 989)	
Oral route	781 (79.0)
Parenteral (IM/IV) route	183 (18.5)
Transdermal route	22 (2.2)
Ocular (eye) route	2 (0.2)
Nasal route	1 (0.1)
Classes of medications prescribed (n = 989)	
Anti-infective drugs for systemic use	423 (42.8)
Drugs working on the musculoskeletal system	197 (19.9)
Drugs working in the alimentary tract and metabolism	112 (11.3)
Drugs working in the blood and blood forming organs	66 (6.7)
Drugs working on the skin	54 (5.5)
Drugs working on the respiratory system	40 (4.0)
Drugs working as antiparasitic products, insecticides and repellants	24 (2.4)
Drugs working on the nervous system	4 (0.4)
Drugs working on the sensory organs (eyes, ears, tongue, skin and nose)	4 (0.4)
Drugs working in the genitourinary tract	3 (0.3)
Others	62 (6.3)

Average duration of therapy, 6.28 ± 1.97

One hundred and sixty (70.5%) of all 227 prescriptions evaluated contained at least a pDDI. In all, a total of 307 pDDIs were detected, of which 210 (68.4%) were noted to be therapeutically desirable, while 97 (31.6%) were non-desirable. Furthermore, 25 (25.8%) and 72 (74.2%) of all the non-desirable interactions were noted to exhibit tendencies to reduce the effectiveness of therapy and adverse events, respectively. Moreover, for the possible cases of adverse events encountered, the cardiovascular system (29, 40.3%), followed by the central nervous/respiratory system (25, 34.7%), and to a lesser extent the renal system (18, 25.0%) accounted for the main organ-systems impacted in the body. On the average, 0.93 ± 0.82 and 0.42 ± 0.77 ($p < 0.05$) desirable pDDI and non-desirable pDDI, respectively were observed per encounter. Both of these translated to 1.35 ± 1.28 pDDI per encounter (Table 4).

Table 4: Potential Drug-Drug Interactions encountered and their therapeutic implications

Characteristics of Drug Drug Interaction	N (%)
Presence of at least a pDDI in a prescription (n = 227)	
Yes	160 (70.5)
No	67 (29.5)
Total number of pDDIs (n = 307)	
Number of desirable pDDIs	210 (68.4)
Number of non-desirable pDDIs	97 (31.6)
Possible clinical consequences of the non-desirable pDDIs (n = 97)	
Reduction in effectiveness of therapy	25 (25.8)
Adverse events	72 (74.2)
Potential adverse events (n = 72)	
Cardiovascular disorder	29 (40.3)
Central nervous/Respiratory disorder	25 (34.7)
Nephrotoxicity	18 (25.0)
Average values of pDDIs encountered	**Mean ± SD**
Average number of all pDDIs per encounter	1.35 ± 1.28
Average number of desirable pDDIs per encounter	0.93 ± 0.82†
Average number of non-desirable pDDIs per encounter	0.42 ± 0.77†

†p < 0.0001

An average of 4.37 ± 1.73 drugs were prescribed for each of the children treated. Meanwhile, percentages of encounters with antibiotics and injections prescribed were 27.8 and 19.2%, respectively, while 642 (64.9%) of all drugs prescribed were written in their generic names (Table 5).

Table 5: Selected prescribing indicators

Indicators		"Standard values ┴"
Average number of drugs prescribed per encounter, (mean ± SD)	4.37 ± 1.73	(1.6 – 1.8)
Percentage of encounters with antibiotics, (%)	27.8	(20.0 – 26.8)
Percentage of encounters with injections, (%)	19.2	(13.4 – 24.1)
Percentage of drugs prescribed by their generic names, (%)	64.9	100

┴ Standards culled from the report by Isah *et al.*[9]

DISCUSSION

Most of the paediatric cases seen in this study were treated as out-patients. They were mostly females and within the age range of 1 - 23 months. During the study period, majority of the children presented with 2 - 3 diseases, most of which were infections, diseases of the digestive system, and diseases of the skin among others. Majority of the subjects were prescribed 4 medications per encounter. Medications were prescribed mostly for 5 days' duration, and majorly by oral and parenteral routes of administration. Among all drugs prescribed, those working as anti-infective for systemic use, on musculoskeletal system, and in the alimentary tract were the most encountered. Majority of all prescriptions vetted contained at least a pDDI, and most were potentially desirable, therapeutically. However, all selected prescribing indicators evaluated were not within referenced standards, except percentage of encounters with injections prescribed.

Majority of the children encountered within the study period were treated as outpatients, probably in keeping with the fact that it is more economical for patients to report from home to the clinics for treatments.[12] This, in a way particularly suites the economic status of majority of the locals who frequent the study center for healthcare services, as suggested by poverty head count rate in Bayelsa State, which has been put at 22.6%.[13] It is important to however note that the graveness of a patient's condition often have a bigger role to play as to whether they will be treated as outpatients or in-patients.[14]

The observation that more female children were brought to the clinic within the study period contradicts that which was reported in United Kingdom by Baker.[15] Meanwhile, it is a general belief that owing to differences in gender-related biological consequences of illness, females tend to suffer from an array of certain types of diseases more than males.[16] This probably explains why more female children than males were presented for treatment at the health facility studied.

It was observed that majority of the subjects who were seen in this study presented with 2 - 3 disease conditions per encounter, which suggests high rates of disease burden among the children in the community hosting the health facility visited. In fact, it has been reported that the youngest and the oldest in the society account for the groups with the highest burden of diseases in a typical population.[17] Of all diseases treated among the children, infectious or parasitic diseases were the most encountered. These have been proven to be widespread among children particularly in developing countries, and are mostly reported as malaria, pneumonia, and diarrhea, among others.[18,19] Other diseases appreciably diagnosed among the children seen included diseases of the digestive system and diseases of the skin among others, which have been reported to be prevailing among the very young individuals in different climes.[17,20]

In treating diseases diagnosed among the children, majority of the subjects received 4 medications at average of 4.37 ± 1.73 per encounter, which passed for several definitions of paediatric polypharmacy as observed in a report by Bakaki *et al.*[18] In order to arrive at a consensus concerning description of what constitutes polypharmacy in drug prescribing for paediatric population, Bakaki and associates[18] conducted a scoping review, and concluded that most reports favour defining paediatric polypharmacy as "the use of two or more concurrent medications or therapeutic classes for one day". Meanwhile, almost all medications prescribed were intended for oral route, and were distantly followed by those prescribed for parenteral route of administration similar to findings elsewhere.[21] In fact, the oral route is considered as the most ideal means of drug administration for long term treatments in children, while the parenteral route is reserved for neonates and emergency cases.[22]

Expectedly, anti-infective drugs intended for systemic use were the most prescribed, obviously in response to high rates of infectious or parasitic diseases diagnosed among the paediatrics assessed, as already related above. This finding is similar to that reported by Rashed *et al.*[23] Similarly, Biradar *et al.*[24] also reported anti-infective agents as the most utilized among paediatric patients studied in Karnataka in 2019. Other medications that were equally prescribed for the children in several encounters were those working on the musculoskeletal system, as well as those that exhibit their activity in the alimentary tract and on metabolism as required by the diseases that were treated. Meanwhile, it has been noted that analgesics, which work on the musculoskeletal system are widely employed for pain management in paediatrics in Africa[25] and in Europe.[26] A similar trend has been reported for medications that work in the alimentary tract and metabolism in some neonatal units in Europe.[27]

That most of the pDDIs seen in this study were noted to be therapeutically desirable corroborates the established fact that cases of drug interactions can actually lead to

desired clinical effect(s) in a given condition.[3,4] Thus, prescribers routinely combine medications in order to exploit the possibility of the foregoing in terms of two or more drugs interacting pharmaceutically, pharmacokinetically or pharmacodynamically. However, some drug interactions may result in reduction in effectiveness of therapy or adverse events, with attendant negative clinical consequences.[3,5] Asides instances of potential reduction in effectiveness of therapy noted for some of the drug interactions observed, appreciable numbers of possible adverse events, affecting mainly the cardiovascular system, central nervous/respiratory system, and the kidney were also noted.

All prescribing indicators evaluated in this study were not within the referenced standards, except percentage of encounters with injections prescribed. This particular finding suggested irrational drug prescribing at the study center, which is similar to the report of a study conducted among under 5 children by Jahan *et al.*[28] at selected primary healthcare centers (PHCs) in Qassim, Saudi Arabia.

Some limitations exist for this study. Firstly, cases of pDDIs reported could have been over- or under-reported given that an electronic Application (Epocrates®) was largely relied upon for the identification of virtually all drug interactions encountered. Secondly, just one out of the several health facilities that are located in the LGA was studied. Hence, it is our opinion that findings from this study may not be generalized to the paediatric population in Bayelsa State, and the Niger Delta Region as a whole.

CONCLUSION
Most of the children seen were treated for infections. Each received average of 4.37 ± 1.73 drugs, and most of these were anti-infective agents. Percentage of encounters with injections prescribed was the only prescribing indicator within referenced standards. Majority of all prescriptions vetted contained at least a pDDI. In all, over a third of all pDDIs observed were non-desirable. Therefore, it is important that prescribers who attend to paediatric patients at the health facility studied be made to adhere to rational prescribing practice as enshrined in the current drug prescribing guidelines for children.

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