Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2021.72945.2198 Volume 30, Issue 3, May 2024
**Manuscript ID ZUMJ-2104-2198 (R4)**
**DOI 10.21608/ZUMJ.2021.72945.2198**
**ORIGIONAL ARTICLE**

# An Audit of Rational Use of Antibiotics in Pediatric Department Zagazig University Children's Hospital

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Submit Date 2021-04-18
Revise Date 2021-08-22
Accept Date 2021-09-23

**Abstract**

**Background:** Antibiotics are one of the most widely used drugs in hospitals, but they are often misused. The proper antibiotic use improves medication and patients' safety, lowers drug intake, costs and reduces the proliferation of resistant species. **Aim and objectives:** To determine the magnitude of inappropriate antibiotic prescription at Zagazig University Children's Hospital. **Methods:** This cross-sectional study was carried out in the pediatric department, faculty of medicine, Zagazig university on 1000 children. All patients were subjected to full medical history with stress on age, sex, diagnosis, past history and antibiotic regimen (begin, course, end). The investigations carried out to the patient were recorded. Clinical outcomes after the use of the antibiotics were carefully evaluated and registered. **Results:** 97.29% of the prescribed antibiotics were of the appropriate dose and 94.22% were of appropriate interval. 68.67% of the prescribed antibiotics fulfill the guidelines, while 31.32% not fulfill the guidelines. The most frequently prescribed antibiotics are Ampicillin/Sulbactam and 3rd generation cephalosporin while the least prescribed antibiotics are Amoxicillin/Clavulanic and cotrimoxazole. **Conclusion:** Antibiotics misuse and overuse are common, contributing to the rise of bacterial resistance. As a result, the main challenges in prescription of antibiotics are to achieve a rational choice and appropriate use of antibiotics and to recognize their potential problems.

**Keywords:** Audit; Antibiotics; Resistance; Pediatrics.

## Introduction:

Antibiotics are one of the most widely used drugs in hospitals, but they are often misused. Owing to discrepancies in pharmacodynamics and pharmacokinetics, children are between the most vulnerable populations to contact illnesses and experience medication side effects **(1).** Antimicrobial Stewardship refers to a set of coordinated interventions intended to optimize the use of antimicrobials in various settings including outpatient clinics and inpatient healthcare settings **(2).** Auditing of antibiotic prescription is one of the most useful methods to rationalize prescribing practices. The quality of life can be improved by enhancing the standards of the medical treatment at all levels of the health care delivery system. A medical audit oversees the observance of these standards **(3).** An 'audit' is described as a review or assessment of health-care practices and registration with the goal of reviewing the quality of care given to the agreed guideline. Analyzing the prescription practice is considered a part of the medical audit that aims to track, assess, and if possible, recommend changes to clinicians' prescribing habits in order to render healthcare more

reasonable and cost efficient (**3).** The right prescription is provided to the right case at the right moment with the right dosage, according to the (Rule of Right) **(7).** They must also meet the criteria of protection, feasibility, necessity, and efficiency. According to the concept, reasonable drug usage, particularly rational prescription must obtain certain requirements **(4).** In reality, proper antibiotic use improves medication and
cases safety, lowers drug intake, costs and reduces the proliferation of resistant species, all with the intention of bettering care quality **(5).**

**Methods:**

***Type of study:*** An observational study.

***Study setting and time:***

This study was carried out in the pediatric department, faculty of medicine, Zagazig university on 1000 child.

***Study population:***

**Inclusion criteria** : included all children admitted to inpatient departments and aged from birth to 18 years. **Exclusion criteria**: involved the cases whose parents were unwilling to participate. Post-surgical and pre-surgical patients or patients with immunodeficiency were also excluded.

***Methods:*** All patients were subjected to full medical history with stress on age, sex, diagnosis, past history and antibiotic regimen (begin, course, end). The investigations carried out to the patient were recorded. Clinical outcomes after the use of the antibiotics were carefully evaluated and registered. Data collected from the prescription order forms, nursing notes as well as electronic reports. Collected data were also compared with standard international antibiotic policy ( East Cheshire NHS Trust Pediatric Antibiotic Policy) **(http://www.eastcheshire.nhs.uk/ )** (6) Narrow-spectrum antibiotics are active against a selected group of bacterial types. Broad-spectrum antibiotics are active against a wider number of bacterial types and thus, may be used to treat a variety of infectious diseases. Broad-spectrum antibiotics are particularly useful when the infecting agent (bacteria) is unknown (6). The difference between brand name and generic drugs is in the circumstances of producing the drugs. While brand name drug refers to the name giving by the producing company, generic drug refers to a drug produced after the active ingredient of the brand name drug.

***Statistical Analysis:***

The prescriptions were analyzed for the percentage of antibiotics prescribed by generic name, percentage of antibiotics with an injection prescribed, percentage of number of antibiotics prescribed, duration of the treatment, the data was pooled and descriptive analysis done. All the documented data were evaluated by applying different Statistical Analysis like mean, standard deviation. This data was analyzed by using Microsoft Data collection and confidentiality all the data and records obtained during the study kept confidential, till authorization from the parents is obtained, or by an exception of the law. No information given to anyone without permission of the parents.

***Administrative considerations:*** Written informed consent was obtained from the care givers and the legal guardian as well as assent from older children (more than 12 years) after clear explanation of the study and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (Institutional Research Board "IRB"). The work has been carried out in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Results:**

Show the distribution of the study population regarding number of antibiotics. 204 (25.06%) children received one antibiotic, 388 (47.6%) children received two antibiotics, 44 (5.4%) children received three antibiotics and 178 (21.8%) children received four antibiotics because of severe infections ,resistance and some times to cover atypical organisms. **Table 1**

**Table (1):** Distribution of the study population regarding number of antibiotics.

| Number of antibiotics | No. | % | P-value |
|---|---|---|---|
| One | 204 | 25.06% | 0.5 |
| Two | 388 | 47.6% | |
| Three | 44 | 5.4% | |
| Four | 178 | 21.8% | |

Qualitative data was represented as number and percentage. P value was set at <0.05 for significant results & <0.001 for high significant result.

Demonstrated the distribution of the study population regarding spectrum of antibiotics. Broad spectrum antibiotic was prescribed in 74.2% of cases, 0.9% of cases received narrow spectrum antibiotic based on culture and 24.7% of cases received narrow and broad-spectrum antibiotic. **Table 2**

**Table (2):** Distribution of the study population regarding spectrum of antibiotics.

| Spectrum | No. | % | P |
|---|---|---|---|
| Broad | 604 | 74.2% | 0.0075 |
| Narrow | 8 | 0.9% | |
| Broad & Narrow | 202 | 24.8% | |

Qualitative data was represented as number and percentage. P value was set at <0.05 for significant results & <0.001 for high significant result.

Distribution of the prescribed antibiotics according to guidelines was cleared as 97.29 % of the prescribed antibiotics were of the appropriate dose and 94.22% were of appropriate interval. 95.82% of the prescription was in the trade name and only 4.17% were in the generic name. 68.67% of the prescribed antibiotics fulfil the guidelines. 31.32% not fulfil guidelines of egyptian neonatal care protocol for hospital physicians and east cheshire NHS trust paediatric antibiotic policy. **Table 3.**

**Table (3):** Distribution of the prescribed antibiotics according to guidelines.

| | | No. | % |
|---|---|---|---|
| **Prescription name** | **Trade** | 780 | 95.82% |
| | **Generic** | 34 | 4.17% |
| Appropriate dose | | 792 | 97.29% |
| Appropriate interval | | 767 | 94.22% |
| **Fulfil guidelines** | | **559** | **68.67%** |
| **Not Fulfil guidelines** | | **255** | **31.32%** |

Qualitative data was represented as number and percentage.

Distribution of the study population regarding the type of prescribed antibiotics. The most frequently prescribed antibiotics are Ampicillin/Sulbactam and 3rd generation cephalosporin these antibiotics were prescribed empirically while the least prescribed antibiotics are Amoxicillin/Clavulanic and cotrimoxazole. **Table 4**

**Table (4):** Distribution of the study population regarding the type of prescribed antibiotics.

| Antibiotic | No. | % |
|---|---|---|
| Ampicillin/Sulbactam | 658 | 36.9% |
| 3rd generation cephalosporin | 448 | 25.1% |
| Meropenem | 176 | 9.9% |
| Aminoglycosides | 168 | 9.4% |
| Vancomycin | 128 | 7.2% |
| Macrolides | 60 | 3.4% |
| 4th generation cephalosporin | 44 | 2.5% |
| Tigecycline | 34 | 1.9% |
| Ciprofloxacin | 26 | 1.5% |
| Piperacillin/Tazobactam | 14 | 0.8% |
| Colistin | 14 | 0.8% |
| Clindamycin | 12 | 0.7% |
| Amoxicillin/Clavulanic | 11 | 0.6% |

| | | |
|---|---|---|
| Cotrimoxazole | 7 | 0.4% |

Qualitative data was represented as number and percentage.

The outcome of advanced antibiotics use is revealed as Tigecycline was prescribed in 34 cases ,61.7% of them improved and 38.3% died. The second advanced antibiotic,ciprofloxacin was prescribed in 26 cases ,65% improved and 35% died. Colistin was prescribed in 14 cases , 57% improved and 43% died. This outcome was due to the disease progress with proper antibiotic. **Table 5**

**Table (5):** Outcome of advanced antibiotics.

| Advanced antibiotic | Improved | | Died | | P-value |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| **Tigecycline(N=34)** | **21** | **61.7%** | **13** | **38.3%** | **0.1** |
| **Ciprofloxacin(N=26)** | **17** | **65%** | **9** | **34.6%** | **0.5** |
| **Colistin(N=14)** | **8** | **57%** | **6** | **43%** | **0.3** |

Qualitative data was represented as number and percentage. P value was set at <0.05 for significant results & <0.001 for high significant result.

Distribution of antibiotics prescription empirically or culture based is revealed as the largest number of antibiotics perscribed based on culture was in NICU and the least number of antibiotics perscribed based on culture was in GIT unit. **Table 6**

**Table (6):** Distribution of antibiotics prescription empirically or culture based. (No.=814).

| System | Empirical on clinical base | Blood culture based | CSF* culture based | Pleural culture based | Urine culture based | Irrational |
|---|---|---|---|---|---|---|
| **PICU** n=70** | 33 | 9 | 0 | 3 | 0 | 25 |
| **NICU*** n=153** | 81 | 31 | 0 | 0 | 0 | 41 |
| **Respiratory infections (n=215)** | 121 | 5 | 0 | 3 | 0 | 86 |
| **GIT infection**** (n=106)** | 64 | 7 | 0 | 0 | 0 | 35 |
| **Urine tract infections (n=67)** | 17 | 4 | 0 | 0 | 37 | 9 |
| **Other infections (n=203)** | 107 | 33 | 4 | 0 | 0 | 59 |

* Cerebrospinal fluid
**Pediatric intensive care unit
***Neonatal intensive care unit
****Gastrointestinal tract infection

Common reasons for the inappropriate antibiotic use was viral infection. In this table the most common cause of misuse of antibiotics was viral chest infections diagnosed by absence of radiological, lab or clinical evidence of bacterial infection. Other cause of misuse of antibiotics was viral GIT infections diagnosed by absence of blood, mucus in stool, lab, or clinical evidence of bacterial infection. **Table 7**

**Table (7):** Common reasons for inappropriate antibiotic use.

| Provisional diagnosis | Final diagnosis | No. | Reason for inappropriateness |
|---|---|---|---|
| Acute bronchiolitis | Acute bronchiolitis | 45 | Viral infection |
| Asthma exacerbation | Asthma exacerbation | 20 | Absent of radiological, lab* or clinical evidence of bacterial infection |
| Viral pneumonia | Viral pneumonia | 22 | Absent of radiological, lab or clinical evidence of bacterial infection |
| Hyperactive airway | First attack of bronchial asthma | 7 | Absent of radiological, lab or clinical evidence of bacterial infection |
| Stridor for DD** | Viral tracheobronchitis | 6 | Viral infection |
| Provisional diagnosis | Final diagnosis | No. | Reason for inappropriateness |
| Gastroenteritis with moderate dehydration | Gastroenteritis with moderate dehydration | 12 | Absent of blood, mucus in stool, lab, or clinical evidence of bacterial infection |
| Chronic diarrhea | Lactose intolerance | 7 | Absent of blood, mucus in stool, lab, or clinical evidence of bacterial infection |
| Chronic diarrhea | Post enteric Malabsorption | 4 | Absent of blood, mucus in stool, lab, or clinical evidence of bacterial infection |
| Autoimmune hepatitis | Autoimmune hepatitis | 3 | Absent of blood, mucus in stool, lab, or clinical evidence of bacterial infection |
| Gastroenteritis with hypernatremic dehydration | Gastroenteritis with hypernatremic dehydration | 9 | Absent of blood, mucus in stool, lab, or clinical evidence of bacterial infection |
| Provisional diagnosis | Final diagnosis | No. | Reason for inappropriateness |
| Rickets | Vit D resistant rickets | 8 | Absent of clinical or lab evidence of bacterial infection |
| Hyperglycemia | DKA*** | 18 | Absent of clinical or lab evidence of bacterial infection |
| Generalized lymphadenopathy | Viral lymphadenopathy | 4 | Absent of clinical or lab evidence of bacterial infection |
| Convulsion | Epilepsy | 19 | Absent of clinical or lab evidence of bacterial infection |
| Acute haemolytic anaemia for DD | G6PD deficiency**** | 17 | Absent of clinical or lab evidence of bacterial infection |
| Jaundice | Neonatal Jaundice | 22 | Absent of clinical or lab evidence of bacterial infection |
| RD***** | TTN****** | 23 | Absent of clinical or lab evidence of bacterial infection |
| Provisional diagnosis | Final diagnosis | No. | Reason for inappropriateness |
| Nephrotic syndrome | Nephrotic syndrome | 3 | Absent of clinical or lab evidence of bacterial infection |
| Nephritic syndrome | Nephritic syndrome | 6 | Absent of clinical or lab evidence of bacterial infection |

Qualitative data was represented as number and percentage.

*Laboratory
**Deferential diagnosis
***Diabetic ketoacidosis
****Glucose 6 phosphate dehydrogenase deficiency
*****Rspiratory distress
******Transient tachypnea of newborn

## Discussion:

Antibiotics are a popular prescription drug in both the community and the healthcare facilities. Today's health care professionals face a difficult task in selecting suitable antibiotics. Clinical practice recommendations are critical in assisting practitioners in selecting the right treatment options for their patients while avoiding the occurrence of antimicrobial resistance. **(5).** The key issues with antibiotics are selecting the right medication for the right indication, dose, and period of treatment to produce the best results. Antibiotic usage must be audited to prevent misuse and the growth of antibiotic resistance. **(8).** Regarding the distribution of our study population according to the number of antibiotics;(47.6%) patients received two antibiotics, that is agree with a study of Khaled and colleagues that was conducted in Saudi Arabia and said that the largest number of patients received at least two antibiotics. **(9).** As regard spectrum of antibiotics, we observed that the majority of patients received broad spectrum antibiotics (74.2%) and this was in a line with Versporten and colleagues **(10).** Considering the type of the prescribed antibiotic, the most frequently prescribed antibiotics were Ampicillin/Sulbactam and 3rd generation cephalosporin. On the contrast to our results, Deshmukh showed in his study that the most commonly prescribed antibiotics were cefixime and followed by amoxicillin-clavulanic acid combination from penicillin group (**11).** Regarding the distribution of the prescribed antibiotics according to guidelines, 68.67% of the prescribed antibiotics fulfill the guidelines but 31.32% didn't fulfill the guidelines of Egyptian Neonatal Care Protocol for Hospital Physicians (ENCPHP) and East Cheshire NHS Trust Paediatric Antibiotic Policy (ECNTPAP) ( http://www.eastcheshire.nhs.uk/ ). Our percentage of irrationality (31.32%) is less than noted in other study was done by Tasawer and others where (43%) of antibiotic prescription was prescribed inappropriately **(12).** Antibiotic misuse is a significant contributor to antimicrobial resistance. The prescribing of antibiotics by physicians based on past experience, without regard for clinical symptoms or para-clinical examinations, is one of the most common causes of improper antibiotic use, leading to a rise in antimicrobial resistance incidence and antibiotic therapy costs **(13).** Regarding the distribution of antibiotics prescription either empirically or culture based, we found that the majority of cases that received empirical antibiotics had respiratory infections while the majority of cases that received culture-based antibiotics were in NICU. According to a report, the majority of patients were given empirical care for LRTI, which they had recommended. However, prescribing antibiotics based on antibiotic susceptibility patterns may be more acceptable**.(14).** In our study advanced antibiotic like Tigecycline was prescribed for 34 cases (4.1%), out of them 21 (61.7%) improved and 13 (38.3%) died. Tigecycline is the first antibiotic in the modern Glycylcycline class of extended broad-spectrum antibiotics, and it has a wide in vitro activity spectrum. It binds to the 30S ribosomal subunit, which inhibits bacterial protein synthesis (**15).** We searched for the common reasons for inappropriate antibiotic use during our study. We found that these reasons may be false diagnosis as in viral infections, absence of radiological, lab or clinical evidence of bacterial infection. Out of the 1000 child included in the study, 814 (81.4%) had an antibiotic prescription, 559 (68.7%) had rational prescription and 255 (31.3%) had irrational prescription according to the guidelines of (ENCPHP) and (ECNTPAP).

Antibiotic usage is affected by physicians' preferences, prior experience with antibiotics, drug availability, and pharmaceutical industry advertising. Despite a growing consensus that a significant portion of antibiotic usage is unacceptable, worldwide use of antibiotics has grown. [16]

## Conclusion and recommendations:

Policy-relevant interventions to combat inappropriate medicines use have generally had

small effects. In the case of antibiotic drugs this may be because the determinants of use, particularly in developing countries, have not been sufficiently understood or addressed. So, it is a must to promote prudent use of antibiotic drugs to minimize the development of resistance. In conclusion, the main challenges in prescription of antibiotics are to achieve a rational choice and appropriate use of antibiotics and to recognize their potential problems. Consequently, physicians must keep a clear understanding need for microbiological diagnosis, use of antibiotics and make good judgment in clinical situations.

We recommend the strict adherence to antibiotics prescription guidelines to overcome the problem of the inappropriate use of antibiotics and thus the great threaten of antimicrobial resistance

**Conflict of interest:** None.
**Funding sources**: None.

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## To Cite :

**Saad Zagloul, S., Hamdy, S., Elsaadany, H., Ramadan, R. An audit of rational use of antibiotics in pediatric department Zagazig university children's hospital. Zagazig University Medical Journal, 2024; (761-768): -. doi: 10.21608/zumj.2021.72945.2198**