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Original Article

Qualitative evaluation of antibiotic usage in pediatric patients

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Abstract

Background Antibiotics are among the most commonly prescribed drug for pediatric patients. Inappropriate use of antibiotics can increase morbidity, mortality, patient cost and bacterial antibiotic resistence. Antibiotic uses can be evaluated quantitatively and qualitatively.

Objective To qualitatively evaluate antibiotic use in patients using Gyssens algorithm.

Methods We performed a descriptive, retrospective study of patientmedical records of those admitted to the pediatric ward from January 1 – June 30, 2009.

Records were screened for patient antibiotic use, followed by qualitative evaluation using Gyssens algorithm on data from patient who received antibiotic treatment.

Results We found 49.2% of subject were prescribed antibiotics. The majority of patients given antibiotics were aged 1 month - 1 year (39.3%). Antibiotic use was categorized by therapy type : empirical, prophylactic, or definitive. We found empirical therapy in 73% of cases, prophylactic in 8%, and definitive in 15%. Cefotaxime was the most common antibiotic used (25.1%), followed by ceftazidime (14%) and cotrimoxazole (1%). 39.6% of subjects were given antibiotics appropriately, while 48.3% were given inappropriately. In 3.3% of patients, antibiotics were given without indication and in 8.8% there was insufficient data.

Conclusions Of hospitalized patients receiving antibiotic treatment at the Departement of Child Health, Cipto Mangunkusumo Hospital, 39.6% were given antibiotic appropriately, while 48.3% were given antibiotics inappropriately. Cefotaxime was the most commonly used, as well as most inappropriately given antibiotic. **[Paediatr Indones. 2011;51:303-10]**.

Keywords*: antibiotic, children, qualitative evaluation, Gyssens algorithm.*

Antibiotics are among the most frequently prescribed drugs for pediatric patients. They are mostly prescribed as empirical therapy, rather than prophylactic or definitive therapy. There have been fewer studies on antibiotics use in children than in adultpatients.[1,2] Inappropriate and unnecessary use of antibiotics increases morbidity and mortality, medical expences and microbial resistance. Inappropriate use of antibiotics is frequently seen in developed countries as well as developing countries.[3,4]

The World Health Organisation (WHO) Global Strategy fo Containment of Antimicrobial Resistance (2001) initiated a program to reduce the expansion of antibiotics resistance.[5] Indonesia, as one of the WHO nations, also participated by conducting a study in 2000-2004 called Antimicrobial Resistance in Indonesia: Prevalence and Prevention (AMRIN) Soetomo Hospital Surabaya and Kariadi Hospital Semarang. The purpose of the AMRIN study was to create a standardized program to acces antibiotics resistance, qualitative and quantitative use of

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antibiotics, as well as control of nosocomial infection, with the expectation that the finding would be applied in all hospitals in Indonesia.

Evaluation of antibiotics use may be conducted to obtain the amount of antibiotics used (quantitative) and antibiotics appropriateness based on the choice of antibiotics, dosage, and duration of administration (qualitative). Quantitative evaluation of antibiotic use is expressed by defined daily dose (DDD)/100 patients -days. Qualitative evaluation by Gyssens algorithm has been widely used in many countries to evaluate the use of antibiotics.[5] Since 2009, Cipto Mangunkusumo Hospital (CMH) has had an antibiotic resistance restrain (program PPRA, team and a map of microbial patterns and antibiotic sensitivities.[6] However, the use of antibiotics in the inpatient unit of Child Health of CMH has never been evaluated in accordance with the PPRA standard, leading us to question its level of appropriate antibiotic use. The purpose of this study was to evaluate the use of antibiotics in the patients ward of Childs Health Departement of CMH qualitatively utilizing the Gyssens algorithm.

Methods

We conducted a descriptive, retrospective study using the medical record of patients treated in the pediatric ward of Child Health Departement to evaluate the appropriateness of antibiotic use. This study was approved by the Research Ethics Committee at the University of Indonesia Medical School.

Subjects were patients aged 1 month to $\leq$ 18 years who received antibiotics therapy and were hospitalized in Class II or Class III inpatients units of the pediatric ward from January 1, 2009 to June 30, 2009. We excluded those treated for less than 24 hours, those receiving topical antibiotics such as eye drops or ointment, those receiving only antituberculosis agents, and those treated in the ICU and neonatal ward.

We completed the research forms, which included demographic characteristics (health insurance, age, gender, inpatient unit, duration of treatment), working diagnosis, antibiotic data including type of antibiotics, route of administration, dosage, frequency, duration of administration, culture results and microbial resistance. Culture results refers to cultures conducted prior to antibiotic use. Repeated cultures were not included in this study. We categorized subjects into surgical and non-surgical cases. Surgical cases were categorized into clean, contaminated clean, contaminated, and unclean. Antibiotics usage was categorized into empirical, prophylactic, definitive or undefined. We used previous, published studies to asses rational antibiotic usage in addition to Gyssens algorithm (**Figure 1**).[7,8]

We evaluated antibiotic usage based on the amount administered during treatment, not the number of patients. We assumed diagnosis in the medical records were correct. Based on Gyssens algorithm, antibiotic use was classified into six categories. I for appropriate use, II a, b, c for inappropriate dosing, interval, route of administration, III a, b for inappropriate treatment duration too long or too short, respectively, IV a, b, c, d for availability of safer, cheaper, more effective, or more spectrum specific antibiotics campared to the ones used in the cases, respectively, V no indication and VI for incomplete medical records. We compared the results first and second assessor (previosily briefed by head of PPRA) with conclusions made by the infectious disease consultant and head of PPRA.

All data in this study was analyzed with SPSS version 17.0. Agreement between the first and second assessor was analyzed using kappa coefficient.

Results

We obtained data from 774 patients, with 415 antibiotic courses used. The algorithm shown in **Figure 2**.

The mean age of patients was four years, ranging from 1 month to 17 years old. The group receiving the most antibiotics was aged 1 month to 1 year. Duration of treatment ranged from 2-57 days, with mean of 11 days.

We analyzed bacterial culture results taken prior to administration of antibiotics. The total of analyzed antibiotic courses was only 415 but of 455, due to incomplete data. One hundred sixty antibiotic courses (38.5%) were given to patient after culture results were obtained. Sixty eight illness cases (27.9%) were reffered to the Infectious Disease Division for antibiotics administration. 88.1% of patients

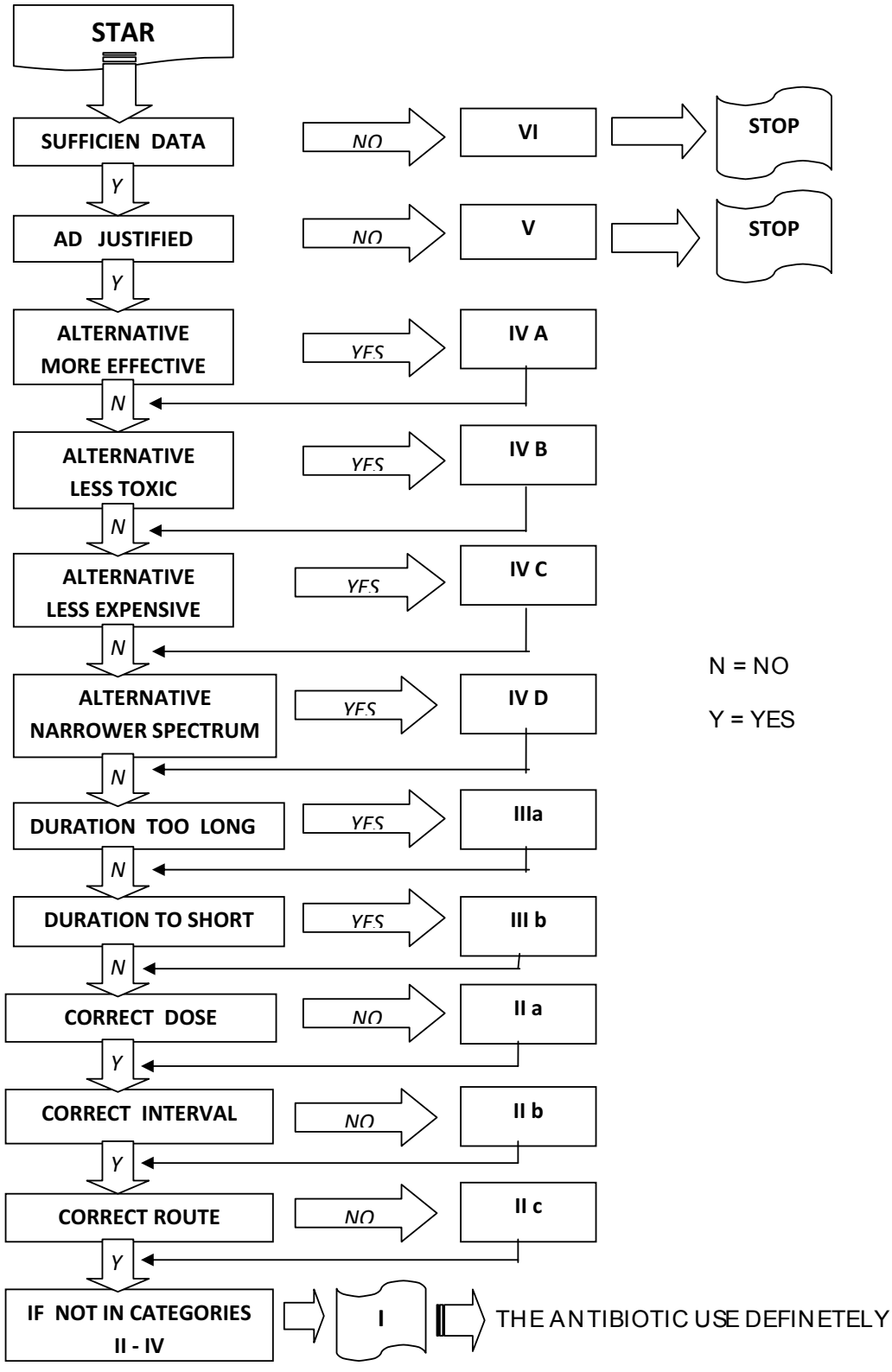

Figure 1. Gyssens algorithm[7]

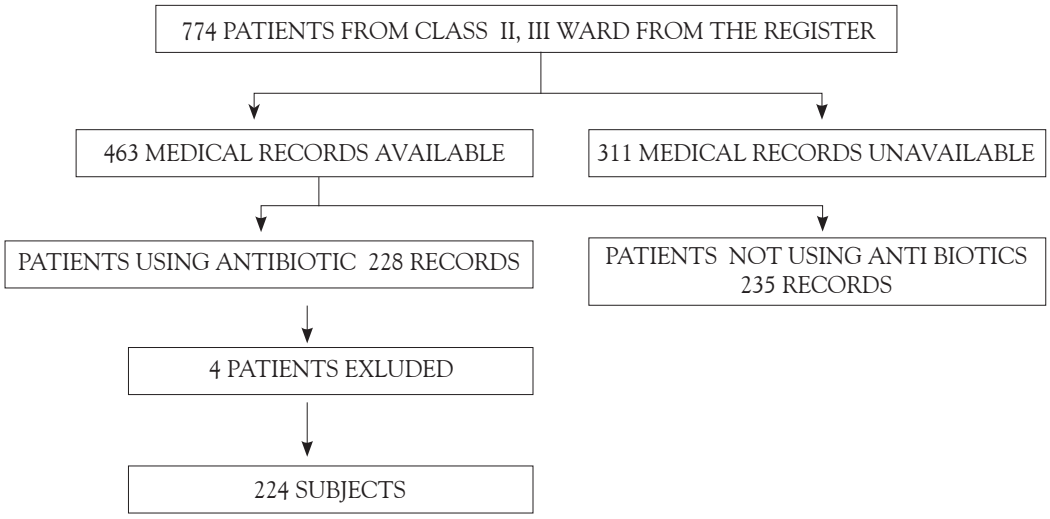

Figure 2. Flowchart of ubject selection

recovered, 5.7% of patients self-discharged against medical advice and 6.2% 6.2% died.

Subjects (n=224) were classified to have surgical or non-surgical illness cases (n=224) (**Table 1**). The were 18 surgical cases (7.4%) and 206 non-surgical cases (92.6%). The higest number of non-surgical cases were from hematology-oncology with 75 (30.8%). Out of these, febrile netropenia was the most frequent ailment (28 cases).

Table 1. Case based illness distribution (n=224)

Case	n	%
Surgery	18	7.4
Neurology	13	5.3
Respirology	39	16
Cardiology	5	2
Gastroenterology	27	11.1
Nephrology	24	9.8
Tropical Infection	42	17.2
Hematology-oncology	75	30.8
Dermatology	1	0.4
Total	244	100

Antibiotics used in this study were categorized according to chemical structure. The most frequently used antibiotics were beta lactams (63.3%), followed by sulphonamide (11%), and metronidazole (8.6%). Appropriate antibiotic use (Category I) accounted for 39.6% of total antibiotic courses, while inappropriated use (Category II,III,IV) accounted for 48.3%. Percentages of antibiotic use under categories V and VI were 3.3% and 8.8%, respectively.

Table 2 shows the distribution of the ten most frequently used antibiotics according to Gyssens algorithm. Cefotaxim was the most frequently used antibiotic (114 courses) in the pediatric ward (25.1%), followed by ceftazidime (14.1%) and cotrimoxazole (11.0%). Cefotaxime was also the most frequently

Table 2. Distribution of the ten most frequently administrated antibiotics according to Gyssens categories

Antibiotics	Gyssens categories						Total
	I	II	III	IV	V	VI	
Cefotaxime	28	16	16	34	7	13	114
Ceftazidime	24	12	5	11	5	7	64
Cotrimoxazole	27	10	9	1	0	3	50
Metronidazole	22	7	5	1	1	3	39
Chloramphenicol	17	5	9	2	0	2	35
Ampisilin	17	2	9	1	0	0	29
Amikacin	5	10	2	4	0	2	23
Ceftriaxone	3	6	1	3	1	2	16
Meropenem	9	3	0	2	0	1	15
Amoxicillin	5	0	4	0	1	2	12

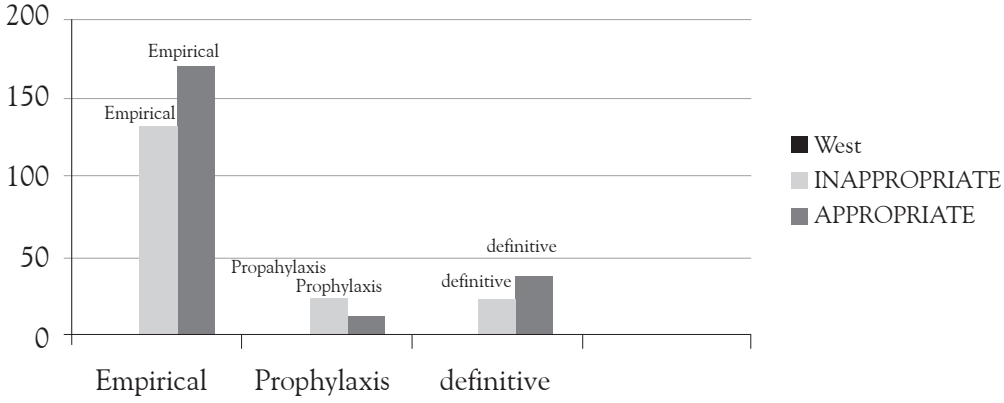

Figure 3. Distribution of antibiotics administration based on indication and Gyssens category.

used antibiotic for all six Gyssens categories.

Total number of antibiotics administered as empirical therapy was 303 (73%), while the ones administered as prophylactic therapy was 35 (8.4%), and as definitive therapy 62 (14.95 %). The most frequently administered antibiotic was cefotaxime for empirical therapy, cotrimoxazole for prophylactic therapy, and meropenem for definitive therapy. Distribution of antibiotic administration based on indication and Gyssens category is shown in **Figure 3**.

A total of 224 cultures performed. We were not found 28 (12.5%) cultures results in the medical record and we were found 196 (87.5%) cultures results. Overall, the most frequent culture results were positive (129), It was representated by 69/196 (35.2%) cultures result , consisting of 20/196 (10.2 %) isolates of *Staphylococcus epidermidis*, 17/196 (8.7%) isolates of Acinetobacter sp, 16/196 (8.7%) isolates of *Escherichia coli* and 16/196 (8.2%) isolates of *Klebsiella pneumonia*.

Based on cultures results , we found there *Staphylococcus epidermidis* 13/196 (6.63%), *Escherichia coli* 15/196 (7.65%) and non pathogenic *Escherichia coli* 6/196 (3.06%) were the most frequently isolated microorganisms in blood, urine and faeces, respectively.

Discussion

In this study, only 59.8% of patient medical records were available. This number was smaller than the number of medical records discovered in Husni's study.[9] in the Child's Health Departement, CMH in 2001 (65%). This low percentage reflects how medical record filing in Child's Health Deparement, CMH still needs improvement. The same problem was encountered in the AMRIN study in the Kariadi and Soetomo Hospitals, which both stated problems regarding medical record filing.[5]

Antibiotics were given to 49.2% of subjects in this study similar to that Husni's study.[9] (48.7%). However, our finding was much lower than that of the AMRIN study, where 90% of patients in the pediatric ward were given antibiotics during their stay.[5] A study in developing and low economic income countries reported that 44%-97% of inpatient are given antibiotics.[10] This may depend on policy of each hospital and may be influenced by the distribution of patient morbidity, which is dominated by infectious diseases in developing countries.

There were more boys than girl in this study. The age distribution ranged from 1 month to 17 year, with mean age of four years. Similarly, Potocki et al found the mean age to 5.1 years old.[11] The age group which received the most antibiotics was 1 month to 1 year, accounting for 39.3% of all subjects.

Duration of hospital stay of the patients ranged from 2 to 57 days, with a mean of 11 days and median of 9 days. We observed a longer duration of stay campare to the study of Shankar et al,[12] who reported a median of 4 days. This was probably due to differences in morbidity distribution in each study. The most frequent antibiotic administrated illness cases in this study were hematology-oncology cases, with febrile neutropenia as the most frequent. However,

Shankar et al[12] found that the most frequent cases (16.6%) to be acute gastroenteritis. Antibiotics were administered after culture results were obtained in 38.5% of antibiotic cources. This observation may be do to financial constraints, as most subjects paid for medical care out-of-pocket (49.6%). Furthermore, cultures were not performed in every case, example in pneumonia cases when diagnosis could be made based on clinical findings.

Consultation by an infectious disease expert on antibiotic choice was done in 27.9% cases. Consultation can increase the rate of proper antibiotics use.[2,13]

The most frequent use antibiotics in our study was for the 75 hematology-oncology cases (30.8%), including for febrile neutropenia (37.3% of hematology-oncology cases), and as prophylactic cotrimoxazole therapy for cancer patients undergoing chemotherapy.

Although the frequency of prescribing antibiotics for children decreased in 1990, the use of broad spectrum antibiotics increased.[2] Consistent with these finding, we observed that of 455 antibiotics courses prescribed, 2 broad-spectrum antibiotics were most frequently used: cefotaxime and ceftazidime (14.1%).

In contrast to our study, Shankar et al[12] found that hospitalized children were most frequently prescribed the antibiotics ampicilin, cefotaxime, and gentamycin. This may be due to the differences in microbial patterns and antibiotic sensitivities in different hospitals and countries.[13]

We found the appropriate use of antibiotics (category I) I 39.6% of antibiotic cources. This number was higher than that of the AMRIN study (21%). We found that the most frequently used antibiotics was cefotaxime (25.1%), and it was also the most frequently inappropriately used. Inappropriate use may be attributed to wrong antibiotics choice (there was a more suitable alternative), dosing, interval, and duration of administration (mainly too long). Too long of a duration, may be caused by failing to evaluate the response to the antibiotic and halting its use. Response towards antibiotics should be evaluated after administration, generally after three days (depending on the diagnosis). If the antibiotics given did not elicit a response, then the possibility of complication, other sources of infection, microbial resistance to the drug, or misdiagnosis should be evaluated.[14]

Rapid use of cefotaxime in the Child's Health Dept. should be reassessed given its low sensitivity (22%) according to "Peta bakteri CMH 2009" (CMH Map of Microbial Patterns).[6] Data from the Clinical Pathology Departement in January- Juni 2009 showed cefotaxime-s sensitivities in the six most frequently isolated bacteria, were 30%, 29%, 8%, 22%, 2%, 27% for *Escherichia coli*, *Staphylococcus epidermidis*, *Acinetobacter sp*, *Enterobacter aerogenes*, *Pseudomonas sp*, and *Klebsiella pneumoniae*, respectively. With these low sensitivities and the absence of a comprehensive guideline on antibiotic use or periodic evaluations, cefotaxime resistance may further increase.

Two studies which evaluated antibiotics qualitatively in a teaching hospital in Thailand reporteds that the percenrage of inappropriate antibiotic prescription was 92% in 1985, but decreased to 26% in 2003.[15,16] These studies shows that with periodic antibiotic evaluation, appropriate use of antibiotics can be promoted.

Antibiotics were most frequently prescribed for empirical therapy (73%). This finding was consistent with study of Van Houten et al.[1] which stated that hospitalized patients most frequently received empirical therapy without evidence of bacterial infection. In our study, this finding was probably due to financial constraints and the fact that culture results takes three to seven days, whereas medications may needs to be administered as soon as possible.

Prescription of antibiotics as prophylactic therapy in this study was 8.4%. This result was lower than that of the AMRIN study (15%). This finding was possibly due to different distribution in subjects morbidity in the two studies. However, prophylactic use in our study was consistent with the study of Shankar et al.[12] in which HIV patients received prophylaxis to prevent opportunistic infections and for cancer patients getting chemotherapy.

Antibiotic prescription as definitive therapy in this study was observed in only 15.5% of antibiotic courses, similar to that observed in developed countries. An American study reported the use of antibiotics as definitive therapy in 20%-25% of patients, while in Holland it was reporteds in 12.3% of patients[1]. This may be caused by the timeneeded to wait for culture results, while medication needs to be administered as soon as possible. In addition even

when there was a culture result, empirical therapy was not always reevaluated. After the microbe is identified and the sensitivity test obtained, definitive therapy should follow.[17]. The use of antibiotics in this study for unknown indications was at 3.3%, lower than that of the AMRIN study (32%).[5]

Inappropriate empirical and inappropriate definitive therapy antibiotic prescription was more frequent than appropriate empirical and appropriate definitive prescription, respectively. Inappropriateness was mostly due to wrong antibiotic choice, mistakes in dosing, and duration of antibiotics administration that was too long. The absence of an antibiotic response reevaluation and the absence of uniformity in dosing guidelines for each disease, may lead to errors of these types, making the creation of uniform antibiotic administration guidelines important. In prophylaxis therapy case, there was more appropriate use of antibiotics compared to inappropriate use. However, this may not be the actual data, given that surgery cases were not further analyzed due to incomplete data.

We found that the majority of Gram positive bacteria isolated from culture was *Staphylococcus epidermidis*. This bacteria is normal flora of human skin and mucosae. Therefore, the possibility of contamination must be considered. To reduce the risk of contamination, it is important to practice aseptic techniques and wash hands properly prior to collecting of culture specimens.

In conclusion, inappropriate use of antibiotics remains a problem encountered by practitioners. It is hoped that health workers will be carefull in choosing antibiotics, including determining the dose, route of administration, and interval, as well as in evaluating clinical response. Cephalosporin use should be considered carefully, especially cefotaxime, since microbial sensitivity is very low (22%). Periodic evalutionis nedd to increase appropriate antibiotic use.

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