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Empirical treatment of neonatal sepsis by *Klebsiella*: A Case study at Komfo Anokye Teaching Hospital (Kath), Ghana

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ABSTRACT

The number of children dying from sepsis in the world has almost doubled in the past 20 years. This is most likely due to the increased number of patients who suffer sepsis. And this may be partly due to the fact that antimicrobial therapy in most developing countries including Ghana is mainly empirical due to a relative lack of appropriate laboratory facilities for culture and sensitivity of bacteria in several health facilities. This study aimed at determining the clinical effectiveness of empirical treatment for neonatal sepsis by Klebsiella at KATH. Eight hundred and two (802) blood specimens from children (in-patients) of age range 1day old to 2years old were cultured on blood agar and MacConkey agar and the isolates investigated. The isolates were identified to the species level using various biochemical tests. The antibiogram of the Klebsiella isolates were determined and compared with the empirical treatment of the patients in the hospital. Klebsiella species were recovered from 51 clinical samples (Prevalence of Klebsiella neonatal sepsis is 6.4%). Gentamicin was the most prescribed agent for the patients (38.7%), amikacin (10.7%), cefotaxime (9.3%), ceftriaxone (8%), chloramphenicol (5.3%), Cot-trimoxazole (5.3%), cefuroxime (4%), Tetracycline (2.6%) and ampicillin (1.3%) for the empirical treatment. Intermediate antibiotic susceptibility pattern was shown by 9.8% of patient's isolates. Also, 37.3% of patient's isolates showed resistance to all the antibiotics used in the antibiotic susceptibility test. Antimicrobial susceptibility was shown by 36 of patient's isolates representing 52.9%. Aminoglycosides and third generation cephalosporins were the most prescribed antibiotics. And although empirical treatment is very relevant, it should be combined with laboratory antibiotic sensitivity testing for effective treatment of Klebsiella neonatal sepsis.

INTRODUCTION

The number of children dying from sepsis in the world has almost doubled in the past 20 years [1]. This may be due to the fact that antimicrobial therapy in most developing countries including Ghana is mainly empirical due to a relative lack of appropriate laboratory facilities for culture and sensitivity of bacteria in several health facilities [2]. Even where laboratory facilities are available, culture and sensitivity tests take 48 to 72 hours to be ready [2], although sepsis requires immediate attention when suspected, therefore initial therapy of patients with possible *Klebsiella* infection is empirical [3]. This usually leads to treatment failure [4]. In this study, we seek to determine the clinical effectiveness of empirical treatment for neonatal sepsis by *Klebsiella* at KATH in Ghana.

MATERIALS AND METHODS

Culture and Isolation

The study was undertaken in the Mother's baby unit (MBU), Pediatric emergency unit (PEU) and Block B (accommodates children) at KATH, Ghana, between May 2007 and March 2008. Blood samples were collected from 802 patients of age range 1day old to 2years old suspected of suffering from sepsis by *Klebsiella*. Demographic data of patients was recorded prior to sample collection. There were no ethical matters concerned with this study, as results from routine laboratory diagnosis of clinical samples constituted the data for analysis; no particular identifiable group of patients were involved and their individual identities could not be traced. The samples were aseptically inoculated on plates of Blood and MacConkey agars (Oxoid Ltd, Basingstoke, UK) and incubated aerobically at 37^{o}C for 24 hours. The morphological characters of the colonies including sizes, shapes, colours, pigmentation and haemolytic nature and microscopic features of the cells were recorded [10]. Suspected *Klebsiella* colonies were isolated and identified through biochemical tests according to Barrow and Felthan [5]. *K. pneumoniae* (NCTC 418. *K. oxytoca* (NCTC 5050 and *Enterobacter aerogenes* (NCTC 10006) were the reference strains employed.

Antibiotic sensitivity test

The Kirby-Bauer agar diffusion method of antimicrobial sensitivity testing [2] was employed to determine the antibiogram of the isolates. The inocula were prepared by growing *Klebsiella* species on Nutrient Agar (Oxoid, UK) plates for 18 h and the colonies formed were transferred into 3 ml of sterile normal saline in a test tube. The density of these suspensions was adjusted to 0.5 McFarland standards. The surface of Muller-Hinton agar (Oxoid Cambridge, UK) plates were evenly inoculated with the organisms using a sterile glass rod. The antibiotic discs from Oxoid Cambridge, UK (ampicillin 10 µg, cefuroxime 30 µg, ceftriaxone 30 µg, cefotaxime 30 µg, gentamicin 10 µg, amikacin 30 µg, co-trimoxazole 25 µg, tetracycline 10 µg and chloramphenicol 10 µg) were placed on the surface of the agar using the antibiotic disc dispenser (Oxoid Cambridge, UK). The plates were then incubated at 37°C for 24 h and zones of growth-inhibition measured and compared to the chart supplied by National Committee for Clinical Laboratory Standards (NCCLS) [6]. Quality control was routinely performed using Escherichia *coli* ATCC 25922. The empirical antibiotic treatments of the patients at the selected babies and children wards were also monitored and the data generated were compared with the sensitivity patterns of the isolates at the laboratory (in vitro).

RESULTS

Klebsiella isolates were recovered from 51 blood samples with prevalence of 6.4%. Mother's baby unit (MBU) registered 21 cases whereas Pediatric emergency unit (PEU) and Block B recorded 15 cases each. As presented in Table 1, gentamicin was prescribed for 38.7% of patients, amikacin for 10.7% of patients, ceftriaxone for 8% of patients, cefotaxime for 9.3% of patients, cefuroxime for 4% of patients and chloramphenicol for 5.3% of patients. Ampicillin was prescribed for 1.3% of patients, Cot-trimoxazole for 5.3% of patients and Tetracycline for 2.6% patients. These antibiotics were prescribed either as monotherapy or in combination with other antibiotics.

Table 1. Number of times prescribed and the sensitivity patterns of the antimicrobials used in the empirical treatment

Antibiotics	No. of times prescribed	%	Sensitivity pattern against *Klebsiella*		
			R	I	S
AMP	1	1.3	1	0	0
TET	2	2.6	2	0	0
COT	4	5.3	2	2	0
GEN	29	38.7	14	2	13
AMK	8	10.7	2	1	5
CRX	3	4	2	1	0
CTR	6	8	2	2	2
CTX	7	9.3	2	1	4
CHL	4	5.3	2	2	0
CHL	4	5.3	2	2	0
CIP	3	4	NT	NT	NT
FLO	2	2.6	NT	NT	NT
FLU	6	8	NT	NT	NT

R-Full resistance, I-Intermediate resistance, S-Susceptible, NT-Not tested.

As indicated in Table 2, intermediate antibiotic susceptibility pattern was shown by 9.8% of patient's isolates. Also, 37.3% of patient's isolates showed resistance to all the antibiotics used in the antibiotic susceptibility test. Antimicrobial susceptibility was shown by 36 of patient's isolates representing 52.9%. This percentage may be higher since three antibiotics; ciprofloxacin (CIP), flucloxacillin (FLU), and floxacillin (FLO) were prescribed for 4%, 2.6% and 8% of patients respectively outside the ones whose susceptibility patterns were tested in the laboratory. This was because the Medical Doctors in charge of the Wards in which the study was done were not informed about the study in order not to influence the treatment pattern. In most cases, they were prescribed in combination with the antibiotics used in this research.

Table 2. Sensitivity patterns of the 51 isolates to the antimicrobials used for the empirical treatment

Sensitivity	Number of isolates	%
Susceptible	27	52.9
Intermediate	5	9.8
Resistant	19	37.3
Total	51	100

DISCUSSION

Empirical treatment is very important in the management of neonatal sepsis in our hospitals since it requires immediate attention when suspected. But in view of the fact that the causative agent may be resistant to the prescribed antibiotic, it is advisable to carry out laboratory sensitivity testing so that medication can be switched when the empirical treatment fails, in order to minimize treatment failures. In this study, we investigated the effectiveness of empirical treatment on *Klebsiella* neonatal sepsis and the appropriate antibiotics that can be used in empirical treatment. Gentamicin was the most prescribed antibiotic followed by amikacin, cefotaxime and ceftriaxone, although amikacin was found to be the most effective drug for *Klebsiella* neonatal sepsis. This could be due to the fact that amikacin is very expensive compared to gentamicin. The isolates of 19 out of the 51 patients, showed resistance to the antibiotics prescribed by physicians in vitro. This puts the prevalence of resistance to antibiotics prescribed at 37.3% which is relatively reasonable compared to other research works by [7] and [8], which reported 37% and 22% respectively as prevalence of resistance. Those which showed only intermediate susceptibility to one or more of the antibiotics used were 9.8% and usually, in the absence of susceptible antibiotics, intermediate susceptible antibiotic is the preferred option.

A marginal increase in the dosage may produce the same effect as a susceptible antibiotic. Also 27 of the patients representing 52.9% had their isolates being susceptible to one or more of the antibiotics used in vitro. This could be higher, since three antibiotics namely ciprofloxacin (CIP), flucloxacillin (FLU), floxacillin (FLO) were prescribed for patients but were not tested in the laboratory (in vitro) and the fact that intermediate susceptibility antibiotics might produce the required results in the patients whose isolates showed intermediate susceptibility to the antibiotics used. Other studies on empirical treatment didn't show much departure from the results obtained in this study. A study on empirical antibiotic treatment at Tel-Aviv, Isreal by [9] revealed that, second generation cephalosporin was prescribed for 34% of patients, third generation cephalosporin for 15% of patients and 63% of the isolates were susceptible to antibiotics used. Another empirical treatment study in Denmark by [8] had high susceptible isolates of 78%.

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