RESULTS

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The present study included 75 children aged from 2-12 years. They were suffered from acute suppurative otitis media or acute otitis media on top of chronic and diagnosed by pneumatoscope in Outpatient Clinic of El-Ahrar Zagazig General Hospital and had temperatures of 38.5°C or greater with no other focal symptoms.

This study was started at September 1992 and end at January 1993.

Blood samples and nasopharyngeal swab samples were taken for complete bacteriological examination.

The results were as follows :

Three types of microorganisms were isolated from the nasopharyngeal samples and they included, S. pneumoniae, B. catarrhalis and S. aureus, as illustrated in table (1).

Table (1)

Number and types of organisms isolated from 75 nasopharyngeal swabs

Organism	From non bacteremic	%	From bacteremic	%	Z	P
S. pneumoniae	39	52	3	4	5.7	<0.05
B-catarrhalis	61	81.3	2	2.7	11.9	<0.05
S. aureus	58	77.3	8	10.7	6.5	<0.05
Total No. of cases (75)	62 (cases)		13 (cases)			

This table illustrated that 56% of cases had S. pneumoniae in their nasopharynx, 4% of which causes bacteremia and there was significant association between the presence of organism in the nasopharynx, and occurence of bacteremia as shown by Z test. Also there were significant associations between the presence of B-catarrhalis and S. aureus organisms and the occurence of bacteremia as proved by Z test.

Table (2)

Number and percent of cases with and without bacteremia due to otitis media

Otitis media	Number	%
with bacteremia	13	17.3
without bacteremia	62	82.7
Total	75	100

Z = 5.09

This table illustrated that there was a significant correlation between otitis media and the occurence of bacteremia as proved by Z test.

Table (3)

Types No. and percent of isolated organisms Causing bacteremia

group	Type of organism	No	%
A	S. pneumoniae	3	23
B	B-catarrhalis	2	15.4
C	S. aureus	8	61.6
	Total	13	100

Z test

Group matching			Z	P
A	vs	B	0.5	>0.05
A	vs	C	2.2	<0.05
B	vs	C	2.8	<0.05

P < 0.05 significant P > 0.05 insignificant

This table illustrated that there was an association between the type of the organism and the occurence of bacteremia. Bacteremic otitis media due to S. aureus infection is significanly higher in incidence than due to S. pneumoniae and B. catarrhalis and S. aureus is the most common organism causing bacteremia.

S. pneumoniae and B. catarrhlis organisms caused bacteremic otitis media but without significant difference in their incidence.

Table (4)

Number and percent of chloramphenicol resistant organisms Causing bacteremia due to acetyltransferase production

Organism	Resistant	%	Sensitive	%	Total
S. pneumonia	2	66.7	1	33.3	3
B-catarrhalis	2	100.0	0	0	2
S. aureus	6	75.0	2	25.0	8
Total	10				13

X^2 test = 0.95

P > 0.05 insignificant

This table illustrated that there was insignificant association between the chloramphenicol resistance of microorganisms and the occurence of bacteremia as shown by X^2 test.

Table (5)

Beta and non beta-lactam producing organisms causing bacteremia

Organism	Producers	%	Non producers	%	Total	Z	P
S. pneumoniae	0	0	3	100	3	3.6	<0.05
B-catarrhalis	1	50	1	50	2	0	>0.05
S. aureus	5	62.5	3	37.5	8	1.3	>0.05
Total	6		7		13		

X^2 = 3.52 P < 0.05 Significant

This table showed that the b-lactamase producing strains are important causes in the development of bacteremia and there was a significant association between the B-lactam production and the occurence of bacteremia as proven by tests of significance.

Table (6)

Antibiotic sensitivity Pattern of the isolated organisms

Antibiotic	S.pneumoniae				B.catarrhalis				S. aureus			
	S	%	R	%	S	%	R	%	S	%	R	%
Ampicillin	1	33.3	2	66.7	1	50	1	50	5	62.5	3	37.5
Penicillin G	1	33.3	2	66.7	1	50	1	50	3	37.5	5	62.5
Chloramphenicol	1	33.3	2	66.7	0	0	2	100	1	12.5	7	87.5
Rifampicin	0	0	3	100	2	100	0	0	8	100	0	0
Velosef	2	66.7	1	33.3	2	100	0	0	6	75.0	2	25
Erythromycin	0	0	3	100	0	0	2	100	3	37.5	5	62.5
Sulphonamides	0	0	3	100	0	0	2	100	0	0	8	100

S = Sensitive R = Resistant

This table illustrated relative resistance and sensitivity of S. pneumoniae to ampicillin, Penicillin G and chloramphenicol and they were absolutely resistant to rifampicin, Erythromycin and sulphonamides and B. catarrhalis were absolutely sensitive to rifampicin and velosef and absolutely resistant to sulphonamides. Also S. aureus showed the same pattern (Table 6).

Table (7)

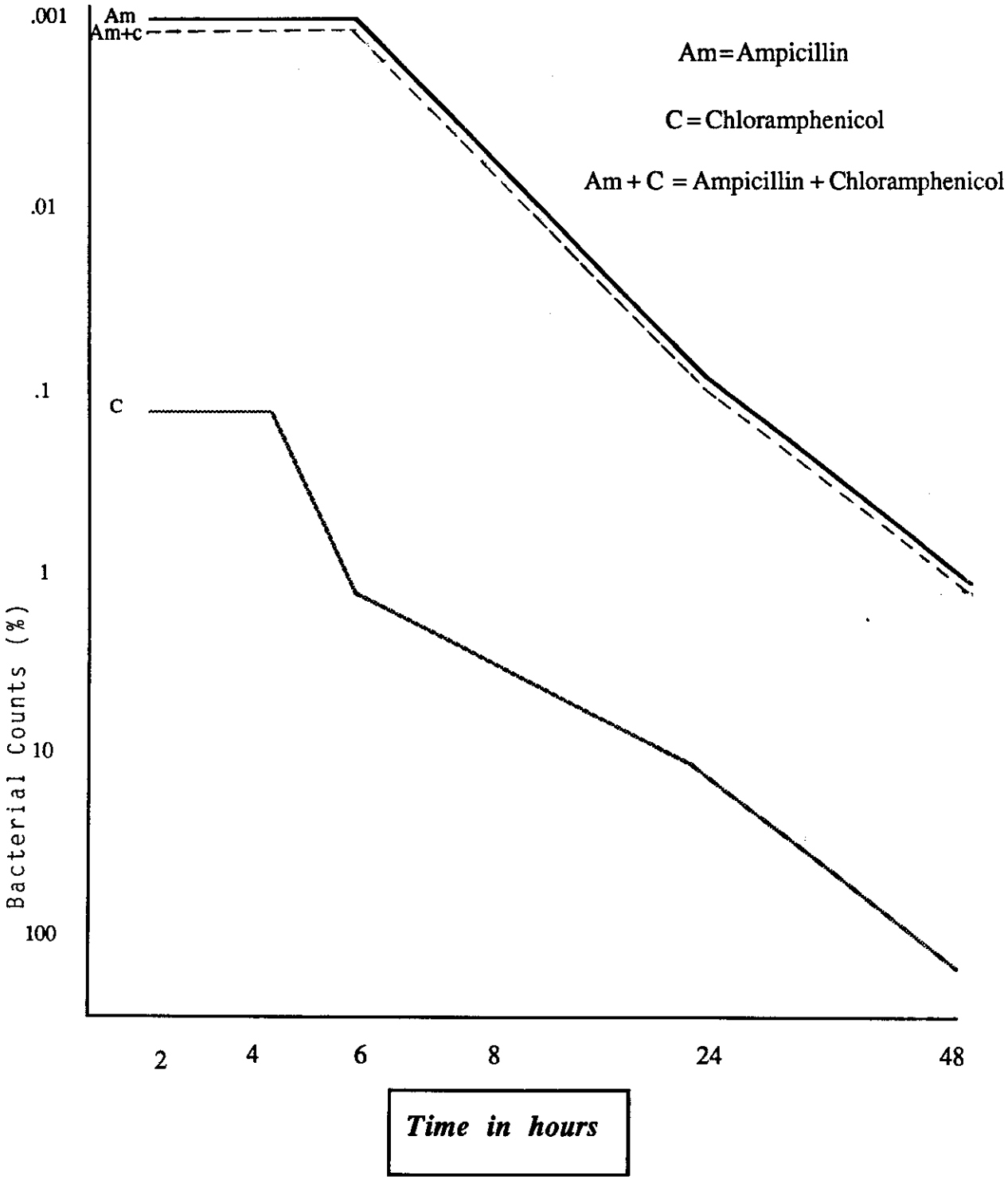
Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of Ampicillin and chloramphenicol of the isolated organisms causing bacteremia

Strain No.	Isolated organisms												
	S. pneumoniae			B. catarrhalis		Staph aureus							
	1	2	3	1	2	1	2	3	4	5	6	7	8
Ampicillin													
MIC	6.25	1.56	0.78	1.56	0.125	0.78	1.56	25	0.39	0.39	0.39	25	0.39
MBC	25	6.25	1.56	6.25	0.39	1.56	6.25	50	0.78	0.78	0.78	50	0.78
Chloramphenicol													
MIC	50	12.5	0.78	25	25	6.25	3.13	25	3.13	6.25	3.13	0.39	3,13
MBC	100	50	1.56	100	50	12.5	12.5	50	6.25	12.5	6.25	0.78	6.25

Table (7) showed that the MIC for S. pneumoniae isolates ranges from 0.78 - 6.25 ug/ml and from 0.78- 50 ug/ml for ampicillin and chloramphenicol respectively and this denoted resistance of this organism to those drugs and B. catarrhalis isolates had MIC between 0.195-1.56 ug/ml for ampicillin and was 25 ug/ml for chloramphenicol and this showed sensitivity for ampicillin and resistance to chloramphenicol and MIC for S. aureus isolates for both ampicillin and chloramphenicol ranged from 0.39 - 25 ug/ml and this showed susceptibility to those drugs.

Fig. (1,2,3) illustrated that the kinetic effect of ampicillin on the isolated organisms which was the same on S. pneumoniae and B. catarrhalis after 2 hrs, 4 hrs and 6 hrs incubation i.e nomultiplication of organisms occur (the bacterial count was at 0.001) after 24 hrs and 48 hrs, the bacterial count rises. The same occured with S. aureus but bacterial counts rises after 4 hrs. The kinetic effect of chloramphenicol in kiling those organisms is less than for ampicillin and bacterial growth occurs rapidly.

These figures also showed that the combined effect of both antibiotics in bacterial killing is the same as ampicillin alone (autonomous effect) and this killing curve is important as the prevalence of ampicillin and chloramphenicol resistance, both drugs should not be used as a single drug therapy of acute otitis media, to avoid therapeutic failure which may cause suppurative complications as bacteremia **(Wyngaarden et al., 1992).**



Fi g (1) : Kinetics of the Bactericidal activities (Kill curve) of ampicillin, chloramphenicol and combined ampicillin, chloramphenicol According to time and Bacterial counts (%) of S. Pneumoniae .

. The ampicillin used is 50 ug/ml and chloramphenicol used is 100 ug/ml

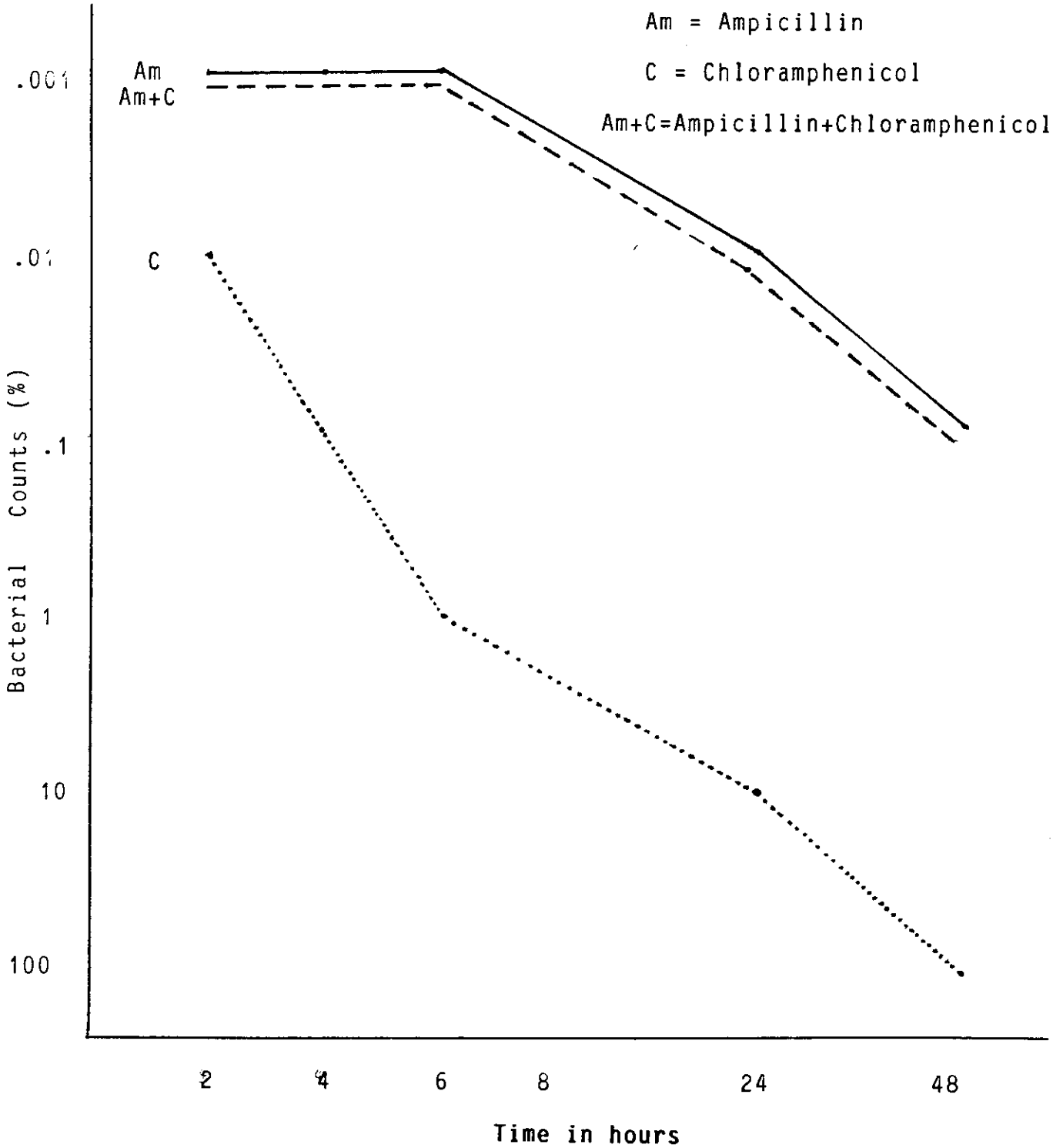


Fig (2) : Kinetics of the Bactericidal activities (Kill curve) of ampicillin, chloramphenicol and combined ampicillin, chloramphenicol According to time and Bacteiral counts (%) of B-Catarrhalis The ampicillin used is 50 ug/ml and chloramphenicol used is 100 ug/ml.

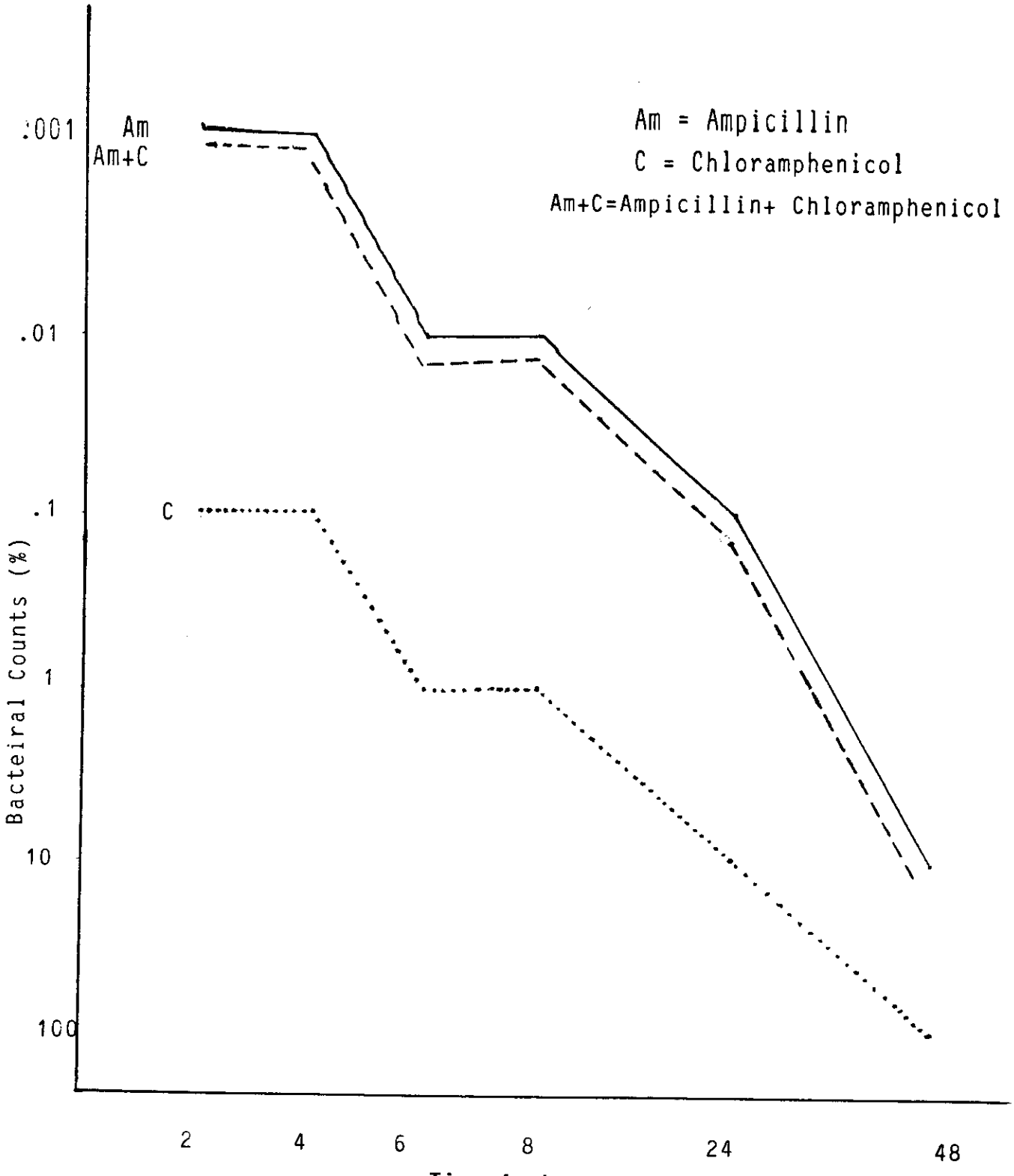


Fig ( ) : KInetics of thge BVactericidal activities (Kil curve) of ampicillin, chloramphenicol and combine ampicillin, chloramphenicol According to time an Bacteiral counts (%) of S. Aureus. The ampicilli used is 50 ug/ml and chloramphenicol used is 10 ug/ml.

DISCUSSION

DISCUSSION

Otitis media is the most common focal bacterial infection of febrile young patients and accounts for a large percentage of both office and emergency visits **(Teele et al., 1983).**

The present study dealt with children aged 2-12 years suffering from otitis media and had temperatures of 38.9°C or greater where nasopharyngeal swabs and blood samples were taken from 75 cases and were subjected to bacteriological study, to determine the causative organisms causing bacteremia with otitis media.

This study isolated 3 types of organisms from nasopharyngeal swabs and from blood samples. They were S. pneumoniae, B-catarrhalis and staph-aureus. There was a significant correlation between organisms isolated from nasopharyngeal swabs and those isolated from blood samples which were the causative organisms causing bacteremia associated with otitis media, this result was not coincided with **Harding et al. (1973)** who reported that there were poor correlations between results of bacterial cultures of the nasopharynx or the oropharynx and those cultures of middle ear fluids to diagnose otitis media but if the patient is toxic as in cases of otitis media associated with bacteremia, culture of the blood should be performed to prove this correlation.

The present result was coincided with **Schwartz et al. (1979)** who reported a correlation between the organisms found in the nasopharynx and those causing otitis media and isolated from the middle ear. Also **Lim and DeMaria (1982)** reported that there was a higher incidence of bacterial colonization (pathogens) in the nasopharynx among patients with histories of acute otitis media (90 percent) as well as chronic otitis media with effusion (80 percent). Compared with low incidence (2 percent) of nasopharyngeal colonization of normal patients, our study illustrated a higher incidence of bacterial colonization (pathogens) in the nasopharynx among patients with otitis media which may cause bacteremia where S. pneumoniae were isolated from 56% of nasopharyngeal swabs and this result was coincided with that documented by **Riley and Douglas (1981)** which stated that the pre-school age children serve as the largest reservoir of S. pneumoniae and the incidence of nasopharyngeal carriage is as high as 55-59 percent. Also B-catarrahalis were isolated from 84% of swabs and this incidence was higher than studies done by **Knopp and Hook (1988)** and by **Vaneechoutte and Coworkers (1990)** whom have shown that the organism is found in the upper respiratory tracts of only (1-5% to 4.5%) of healthy adults and is actually more common in the respiratory tracts of healthy children (50.8%) and elderly adults (26.5%). Also S. aureus were isolated from 88% of swabs.

This incidence was higher than that reported by **Wilson and Mills (1975)** whom stated that the throat carriage of staphylococcus aureus in healthy persons was varrying between 4-64%.

The blood samples taken give an idea about the incidence of bacteremia with otitis media in the present study which account for 17.3%. These results was not coincided with that of **McCarthy. et al. (1976)** whom found bacteremia in 45% of a group of outopatients suffering from otitis media and fever of unknown origin, and was not in agreement with that documented by **Teele et al. (1975)** whom reported that 1.5% of children less than 2 years of age with otitis media and temperatures greater than 38.9°C were bacteremic. Also these results differs from that obtained in 1976 by **McCarthy et al.** whom described an incidence of 5.8% and also not coincided with results obtained by **Schwartz and Weintzen (1982)** whom found 5.8% incidence of bacteremia in febrile infants with otitis media and this also do not agreed with **Schutzman et al. (1991)** whom found 3% incidence of bacteremia in a population of patients 3 to 36 months of age with temperatures > 39°C who were diagnosed as otitis media. The results of our study determined three types of organisms. causing bacteremia and they were S. pneumoniae, B-catarrhalis and S. aureus. These results were in agreement with those

obtained by **McCarthy et al. (1977) and Winchester et al. (1977)** whom reported that in children beyond the newborn age groups. S. pneumoniae, H-influenzae type b S. aureus, salmonellae spp. and Neisseriae spp. are the most common microorganisms causing bacteremia.

Our study illustrated that the development of bacteremia is variable and dependant upon the specific microorganisms isolated, where S. pneumoniae and S. aureus organisms are the most common types of organisms causing bacteremia. These results were coincided with those of **Michaels et al. (1977) and Kaplan et al. (1981)** whom stated that the pathophysiology of bacteremia is highly variable and dependant upon the specific microorganisms isolated, We found that S. pneumoniae caused 4% of bacteremia in patients with otitis media. This was very lower to those reported by **Jaffe et al. (1987)** whom found that (50%) of children had bacteremia due to S. pneumoniae in upper respiratory tract infections including otitis media. Also we found that (10.7%) of patients with otitis media were bacteremic due to infection by S. aureus and this was higher than those reported by **McGown et al. (1973)** whom stated that (0.85%) of patients with otitis media had bacteremia due to infection by S. aureus. The present study illustrated that B. catarrhalis caused 2.7% of bacteremia in patients with otitis media and this was

coincided with **Karma et al. (1985)** whom stated that there was no reported bacteremia secondary to otitis media due to B. catarrhalis infection. However **Baron and Shapiro (1985)** found three cases of bacteremia secondary to upper air way disease. The antibiogram for the isolated strains showed that Streptococcus . pneumonia showed variable sensitivity and resistance to ampicillin, penicillin G and chloramphenicol and they were absolutely resistant to rifampicin. Erythromycin and sulphonamides, these results was conformed to those obtained by **Applebaum et al. (1977); Cates et al. (1978) and Ward (1981).** Also B. catarrhalis showed variable sensitivity and resistance to ampicillin and pneicillin and they were absolutely sensitive to rifampicin and velosef and absolutely resistant to chloramphenicol, Erythromycin and sulphonamides. These results were in agreement to those done by **Newing and Christie (1974)** whom recognized the relative resistance of B-catarrhalis to penicillin in Finland and to those reported by **Kallings et al. (1983)** whom found that seven strains of B. catarrhalis in Sweden were resistant to erythromycin these results were also reported from the Neitherland by **Davies and Maesen (1988)** whom reported resistance to erythromycin by this organism. The isolated strains of S. aureus in our study showed variable sensitivity and resistance to ampicillin G, chloramphenicol, velosef and erythromycin and was absolutely sensitive to rifampicin and absolutely

resistant to sulphonamides. These results were in agreement with those reported by **Haley et al. (1982)** whom stated that most strains of S. aureus are sensitive to semisynthetic pencillinase resistant penicillins and cephalosphorins and although after inhibited by such antibiotics as erythromycin and chloramphenicol. S. aureus is not killed by these agents and there they have no place in the therapy of bactreremic infections.

In the present study the b-lactamase producing strains were identified where 62.5% of isolated S. aureus were B-lactam.Positive. These results were in agreement with that of **Kogan (1980)** who stated that the majority of Gram-positive organisms in which the B-lactamase is the sole major factor in resistance and this was in agreement with a study done by **Hoebrich (1983)** who stated that antibiotic treatment of staphylococcal pneumonia is complicated by the fact that approximately (50 percent) of staphylococcal isolates are B-lactamase-positive. In the present study it was found that 50% of isolated B-catarrhalis were B-lactam producers these results were lower in percent than results produced by **Johnson et al. (1981)** whom demonstrated that from a series of seven patients with B-catarrhalis lung infections five of the seven isolates were B-lactam producers in a percent of 71.4%. These results were higher in percent than those reported by

Seinonen et al. (1981) in Finland where the B-catarrhalis is the third commonly pathogen in the middle ear fluid They found that 2.0 percent of the isolates produce B-lactamase and these results were similar to that reported by **Oberhoffer and Towle (1982)** whom stated that the spread of B-lactamase among strains of B-catarrhalis in the United States occured rapidly. Approximately (40 percent) of strains were B-lactam positive, also **Shurin et al. (1983)** reported that the B-lactam incidence of B-catarrhalis reached 75 percent. This coincided also with reports produced by **Wallace et al. (1989)** whom found a similar incidence, also our results were lower in incidence than those reported by **Jorgensen et al. (1989)** whom stated that out of 378 B-catarrhalis recovered from 15of United States medical centers during 1987 to 1988, the B-lactam incidence was 84 percent.

In our study we found that S. pneumoniae isolates were non B-lactamase producers but **Jacobs et al. (1978)** reported that strains of S. pneumoniae possessing high-level penicillin resistance i.e. MICs 100-10.000 times greater than those for susceptible strains, were resistant to all B-lactam antibiotics.

In the present study, the isolated strains were tested for chloramphenicol resistance due to the production

of enzyme acetyl transferase and there was an insignificant correlation between chloramphenicol resistance and the occurence of bacteremia due to thereapeutic failure of acute otitis media. This was coincided with those reported by **Sando and Shaw (1973)** whom stated that resistant strains of S. aureus contain one of several related forms of chloramphenicol acetyle transferase that are inducible and also **Haley et al. (1982)** reported that although S. aureus often inhibited by chloramphenicol, is not killed by this antibiotic and this causes therapeutic failure of acute otitis media. Also **Gaffney and Foster (1978)** stated that resistance of gram-positive and gram-negative micro-organisms is due to the presence of a specific acetyl transferase that inactivates the drug.

In the present study, the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were identified for the isolated organisms for ampicillin and chloramphenicol where the MIC for S. pneumoniae isolates ranges from 0.78 - 6.25 ug/ml and from 0.78 - 50 ug/ml for ampicillin and chloramphenicol respectively and this showed resistance of S. pneumoniae isolated to both antibiotics and this coincided with **Ward (1981)** who denoted that ampicillin resistance is said to occur when MICs are > 4 ug/ml and 3.2 ug/ml for chloramphenicol and therapeutic failure of cases of acute otitis media

occurs when MIC for both drugs exceeds 6 ug/ml as reported by **Applebaum et al. (1977)** and this may cause suppurative complications.

In our study the isolated B-catarrhalis had MIC between 0.195 - 1.56 ug/ml for ampicillin and was 25 ug/ml for chloramphenicol, and this showed sensitivity to ampicillin and resistance to chloramphenicol and this was in agreement with **Ahmad et al. (1984) and Doern and Tubert (1988)** whom stated that the resistant B-catarrhalis will have MIC of 2 ug/ml and this was coincided with those documented by **Standiford (1985)** who stated that over 95% of Neisseria species including B-catarrhalis are inhibited by 6.3 ug/ml of chloramphenicol. In the present study the MIC of S. aureus for both ampicillin and chloramphenicol ranged from 0.39 - 25 ug/ml and this showed susceptibility of this organism to those drugs as that reported by **Koneman et al. (1992)** whom illustrated that when testing S. aureus for ampicillin and chloramphenicol they found that they were resistant at MIC < 32 ug/ml, The kinetics of bactericidal activities (kill curve) of ampicillin and chloramphenicol each by itself and then both were combined showed, by plotting time against bacterial counts that the effect of killing bacteria by ampicillin is more effective than chloramphenicol and the combined effect of

both antibiotics is the same as that produced by ampicillin alone (autonomous effect) and this results were coincided with **Wyngaarden et al. (1992)** whom reported that because of the prevalence of ampicillin and chloramphenicol resistance, both drugs should not be used as a single drug therapy of acute otitis media to avoid therapeutic failure which may cause suppurative complications as bacteremia.