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The Changing Pattern of Causative Bacterial Organisms in Neonatal Meningitis

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Summary

Dawodu AH and Ashiru JO. The Changing Pattern of Causative Bacterial Organisms in Neonatal Meningitis. *Nigeran Journal of Paediatrics* **1983; 10:1.** A retrospective study of 36 infants with bacteriologically proven neonatal meningitis at the University College Hospital, Ibadan, Nigeria, between January, 1976 and June, 1981, has revealed a changing pattern in the causative organisms and their sensitivity. In the present study, gram-negative organisms accounted for 61% of the isolates. Enterobacteria, especially *E. coli* and *Klebsiella* species were the commonest gram-negative agents. No case of *Salmonella* was found. By contrast, *Salmonella* species accounted for 54% of the enterobacteria isolated in a previous study from the same unit. *Pneumococcus* was the leading gram-positive agent and its frequency of isolation has doubled since the last study. Antibiotic sensitivity patterns in the present study suggest that penicillin (or ampicillin) combined with gentamycin should be the initial antibiotics in cases of neonatal meningitis in our environment. The study agrees with previous suggestions that causes of neonatal infections vary from one community to another and change from time to time within the same community or institution. Therefore, a rational approach to antimicrobial therapy can only be based on regular review of the causative agents and their antibiotic sensitivity patterns.

Introduction

THE predominant causative organisms in neonatal meningitis are gram negative enterobacteria of which *Eschericia coli* is the commonest. [1 2 3] A previous report from the University College Hospital (UCH), Ibadan, revealed that *Salmonella* species were the commonest causative agents in neonatal meningitis.[4] Changes in the pattern of actiologic agents in neonatal meningtis have been reported recently from some technically developed parts of the world.[5 6] A review of the antibiotic sensitivities of the causative organisms has led to formulation of optimal antibiotic policy which has contributed to better prognosis.[6] The present retrospective study describes the changing pattern of bacterial agents isolated from the cerebrospinal fluid (CSF) of neonates with meningitis at the UCH and recommends appropriate antibiotic therapy.

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Materials and Methods

The patients included all neonates born in the UCH and those referred from outside to the children's emergency room with bacteriologically proven meningitis, between January, 1976 and June, 1981. Patients with such central nervous system abnormalities as myelomeningocele were excluded. During the period under review, the initial antibiotic therapy routinely administered in many cases of neonatal meningitis was a combination of intravenous ampicilin (100mg/kg/day) and intramuscular (i.m.) kanamycin (15–20mg/kg/day) or i.m. gentamycin (5–7.5mg/kg/day). In some cases, cloxacillin was substituted for ampicillin, if the provisional diagnosis was septicaemia and meningitis since *Staphylococcus aureus* is the most common gram-positive agent responsible for septicaemia in our centre.[7] The above routine antibiotic therapy was modified in each case according to the bacteriological sensitivity reports when these became available. The results of the aetiologic agents, antibiotic sensitivities and mortality rate were then compared with those of a previous study[4] carried out at the same institution between January 1961 and May 1969.

Statistical analysis was by means of chi-squared tests.

Results

There were 36 patients (20 males and 16 females) during the period under review and of these, 18 (50%) presented within the first week of life, six during the second week of life and 12 after two weeks of age.

Aetiologic agents

Table I summarizes the isolated causative organisms. Gram negative organisms were found in 22 (61%) and Gram positive agents in 14 (39%) of the cases. *E. coli* and *Klebsiella* species were the commonest gram negative agents, while *Strep. pneumoniae* accounted for 71% of the gram positive isolates. A comparison of these causative agents with 36 verified cases of neonatal meningitis reported from the same institution[4] in 1971, is summarised in Table II. The striking difference is the absence of *Salmonella* species and the higher incidence of *Pneumococcus* in the present study. The commonest gram-negative organisms in the present series were *non-Salmonella* enterobacteria. Table III shows the relationship between the age at the onset of illness and causative organisms. Gram negative bacilli were the causative organisms in 16 (88.8%) of the 18 infants that presented in the first week of life, while *Streptococcus* was the commonest causative organism after the first week of life.

TABLE I

Causative Organisms in 36 Cases of Neonatal Meningitis

	Organism		*Total No. of Isolates*
A.	Gram-negative		22
	E. coli (8)		
	Klebsiella species (5)		
	Proteus (3)		
	Haemophilus influenzae (2)		
	Alkalagenes Spp (2)		
	Pseudomonas (1)		
	Serratia (1)		
B.	Gram-positive		14
	Streptococcus (11)		
	Strep. Pneumoniae	10	
	Group B. strep.	1	
	Staphylococcus (3)		
	Staph. aureus	2	
	Staph.albus	1	
	Total		36

TABLE II

Aetiologic Agents in Neonatal Meningitis in Ibadan: Comparison between Present and Previous Studies[4]

	Organism	*Present series*		*Previous series*	
		No. of cases	*% of Total*	*No. of cases*	*% of Total*
A.	Gram-negative	22	61.1	26	72.2
	Salmonella	(0)	(0.0)	(14)	(38.1)
	Other Gram-negative	(22)	(61.1)	(12)	(33.3)
B.	Gram-positive	14	38.9	10	27.8
	Pneumococcus	(10)	(27.8)	(5)	(13.9)
	Other	(4)	(11.1)	(5)	(13.9)
	Total	36	100.0	36	100.0

TABLE III

Relationship between Age at Onset of Illness and Causative Organism in 36 Cases of Neonatal Meningitis

Age (days)	*Organism*			*Total No. of cases*
	Gram-negative bacilli	*Strep-tococcus*	*Staphy-lococcus*	
0 - 7	16	1	1	18
8 - 14	3	2	1	6
15 - 21	2	2	1	5
22 - 28	1	6	Nil	7
Total	22	11	3	36

Sensitivity pattern

Of the 20 *Gram negative* isolates tested, only two (10%) were resistant to gentamycin, while 9 (44%) were resistant to chloramphenicol. All the 10 pneumococcal isolates were sensitive to penicillin and ampicillin, while one (10%) was resistant to chloramphenicol. Using the present sensitivity reports, the appropriateness of the initial antibiotic therapy was compiled and summarised in Table IV. If the isolate was sensitive to any of the antibiotics or combination of the antibiotics, the therapy was judged to be appropriate.

Prognosis

Two of the mothers absconded with their infants and the outcome was therefore, unknown. Of the remaining 34 patients, 18 (53%) died (Table V). Nine (50%) of the 18 males and nine (56.3%) of the 16 females died; sex therefore, did not significantly affect mortality ($p > 0.5$). Ten (62.5 %) of the 16 low birthweight (LBW) infants died, compared with eight (44.4%) of the 18 infants with normal birthweight. Although the mortality among LBW infants was higher, the difference was not statistically significant ($p > 0.2$). The case fatality among patients with gram-negative meningitis was higher than that found in patients with pneumococcal meningitis (Table V), but the difference was also not significant ($p > 0.4$). The case fatality rates among patients in the present study was however significantly lower ($p < 0.01$) than that reported previously[4] (Table V).

TABLE IV

Initial Antibiotic Therapy and its Appropriateness in 34 Cases of Neonatal Meningitis

Antibiotics	*No. of Cases*	*No. of Cases adjudged appropriate*	*% of Cases adjudged appropriate*
Penicillin and Cloramphenicol	1	1	—
Ampicillin	2	2	—
Triple therapy (Penicillin chloramphenicol + sulphadimidine	1	1	—
Penicillin and gentamycin	1	1	—
Ampicillin and kanamycin	10	7	70
Ampicillin and gentamycin	7	6	86
Cloxacillin and gentamycin	11	9	82
Ampicillin and cloxacillin	1	0	—
Total	34	27	79

TABLE V

Summary of Prognosis in Relation to Causative Agent: Comparison between Present and Previous Series[4]

Organism	Present series			Previous series			P
	No. of cases	*No. of deaths*	*% Mortality*	*No. of cases*	*No. of deaths*	*% Mortality*	
Gram-negative	20†	13	65	26	24	92	<0.05
Gram-positive	14	5	35·7	10	6	60	NS
Total	34	18	53	36	30	83	<0.01

† excluding two cases whose outcome is unknown.

Discussion

Knowledge of the common causative organisms and their antibiotic susceptibility is necessary for optimal antibiotic management in bacterial infections. This is particularly important in neonatal infections since antibiotics must be started early in order to reduce morbidity and mortality. Furthermore, since the type of organisms causing neonatal infections may change from time to time, [8 9] it is important to be aware of the current causative agents.

The present study has revealed that, in the last decade, there has been a significant change in the type and pattern of antibiotic sensitivities of bacterial agents responsible for neonatal meningitis in our insitution. It is worthy to note that in the present series, no *Salmonella* organisms were isolated from the CSF, while *E. Coli* and *Klebsiella* species were the predominant gram-negative agents. By contrast, of the 26 cases due to gram-negative organisms previously reported from the same institution, 14 (53.8%) were due to *Salmonella* organisms.[4] Furthermore, *Pneumococcal* organisms in the present series were twice as many as those reported previously. Neither the pattern of isolation of the *Salmonella* organisms in the previous study [4] nor that of *Pneumococcus* in the present study was suggestive of an "Epidemic". The reason for this changing pattern in the causative agent is therefore not known, but such a finding has been reported elsewhere.[8 9]

The present findings, however, agree with those from technically developed countries of the world, which showed that non-*Salmonella* enterobacterial agents were the commonest cause of neonatal meningitis. [1 2 3] Recent reports from North America [5 6 10] have implicated Group B beta-haemolytic *Streptococcus* as the leading cause of neonatal meningitis. This constrasts with our findings of *Pneumococcus* as the commonest gram positive agent. There was only one case of Group B beta-haemolytic *Streptococcus* in our series, consistent with the low incidence of Group B beta-haemolytic *Streptococcal* infections among neonates in the environment (unpublished data).

The antibiotic sensitivities of the pathogens isolated in the present study suggest that a combination of penicillin (or ampicillin) and gentamycin is the appropriate initial antibiotic therapy in neonatal meningitis. This initial therapeutic regime would cover about 90% of the causative organisms and had it been used in the present series, it would have increased the percentage of antimicrobial therapy adjudged to be appropriate. It should, however, be emphasised that it is mandatory to follow up laboratory sensitivity report in each case so as to modify the drugs accordingly.

The case fatality rate of 53% in the present study is significantly lower than the 83% previously reported from this institution,[4] but is close to the 60–70% mortality reported from other centres.[2 3] Recently, mortality rates as low as 15–40% have been reported elsewhere, but it should be noted that differences in mortality from neonatal meningitis depend on variable factors including the characteristics of the infant population, aetiologic agents, appropriateness of antimicrobial therapy and the standard of neonatal care. The lower mortality in the present series than those of a previous study from our institution is most likely due to a combination of the above factors. The appropriateness of the initial antibiotics and the lower incidence of resistant organisms to the antibiotics used in the present study probably played a significant role. This is supported by the fact that while only 10% of the common organisms responsible for neonatal meningitis in the present series were resistant to the initial antimicrobial therapy, the figure was as high as 70% in the previous study.[4] The routine initial therapy was then a combination of penicillin, chloramphenicol and sulphadimidine (triple therapy) during the period when the previous review was undertaken. Such a therapy was not adequate for the treatment of neonatal meningitis and could have contributed to the poor outcome. It is also relevant to mention that there were no paediatricians with special training in neonatal care in the hospital during the period of the previous study as compared with that of the present study when such members of staff were available for teaching and supervision. It will therefore be reasonable to suggest that the standard of neonatal care during the present study was better, thus contributing to the lower mortality in the present series.

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