Neonatal septicaemia in the neonatal care unit, Al-Anbar governorate, Iraq

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الإنتان الدموي بين حديثي الولادة في وحدة رعاية المواليد، في محافظة الأنبار، في العراق

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الخلاصة: يُعَدُّ الإنتان الدموي **septicemia** بين حديثي الولادة مُسَبِّباً رئيسياً للوفاة والمراضة في البلدان النامية. وقد تم في هذا البحث دراسة 118 حالة إنتان دموي لدى أطفال حديثي الولادة أُدخلوا مستشفى الإحالة الرئيسي في محافظة الأنبار، في العراق، أظهرت مزرعة الدم إيجابيتهم للجراثيم. وبلغ معدل حدوث الإنتان الدموي بين الأطفال الحديثي الولادة في هذا المستشفى 9.2 لكل ألف من المواليد الأحياء، وبلغ معدل الوفيات بينهم 28٪. وتبين الدراسة أن 90٪ من الجراثيم المستفرَدة هي العنقودية الذهبية (39٪)، والكلبسيلة الرئوية (30٪)، والإشريكية القولونية (21٪). وأظهرت المستفرَدات حساسية في المختبر للسيفوتاكسيم والكلورامفينيكول والجنتاميسين، ولكنها أظهرت مقاومة للمضادات الحيوية الأكثر استخداماً مثل الأمبيسيلين والكلوكساسيلين. وتوصي الدراسة بتقديم معالجة أولية بكل من الجنتاميسين والسيفوتاكسيم معاً ريثما ترد نتائج المزرعة واختبار الحساسية. وتؤكد هذه الدراسة على أهمية فهم الجوانب الوبائية المحلية لحالات الإنتان الدموي بين حديثي الولادة عند صياغة سياسة رشيدة لاستخدام المضادات الحيوية.

ABSTRACT Neonatal septicaemia is a major cause of morbidity and mortality in developing countries. We studied 118 neonates admitted to the main referral hospital in Al-Anbar with positive blood cultures. The incidence of neonatal septicaemia for babies born at this hospital was 9.2 per 1000 live births, and mortality was 28%. *Staphylococcus aureus* (39%), *Klebsiella pneumoniae* (30%) and *Escherichia coli* (21%) constituted 90% of all isolates. The isolates showed *in vitro* susceptibility to cefotaxime, chloramphenicol and gentamicin, but resistance to more commonly used antibiotics such as ampicillin and cloxacillin. We recommend initial gentamicin/cefotaxime combined therapy while awaiting culture and sensitivity test results. Our study highlights the importance of understanding the local epidemiology of neonatal septicaemia in formulating a rational antibiotics policy.

La septicémie néonatale dans le service de soins néonatals, Gouvernorat d'Al Anbar (Iraq)

RESUME La septicémie néonatale est une cause majeure de morbidité et de mortalité dans les pays en développement. Nous avons étudié 118 nouveau-nés admis avec des hémocultures positives dans le principal hôpital de recours du Gouvernorat d'Al Anbar. L'incidence de la septicémie néonatale pour les bébés nés dans cet hôpital était de 9,2 pour 1000 naissances vivantes, et la mortalité s'élevait à 28 %. *Staphylococcus aureus* (39 %), *Klebsiella pneumoniae* (30 %) et *Escherichia coli* (21 %) constituaient 90 % de tous les isolats. Les isolats ont montré un sensibilité in vitro à la céfotaxime, au chloramphénicol et à la gentamicine, mais une résistance à des antibiotiques utilisés plus couramment tels que l'ampicilline et la cloxacilline. Nous recommandons un traitement initial associant gentamicine et céfotaxime en attendant les résultats de la culture et des tests de sensibilité. Notre étude souligne qu'il est important de comprendre l'épidémiologie locale de la septicémie néonatale pour formuler une politique rationnelle en matière d'antibiotiques.

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Received: 26/06/01; accepted: 09/12/01

Introduction

Despite advances in antimicrobial therapy and supportive care, septicaemia continues to be a major cause of morbidity and mortality in the neonatal period. In developing countries, many of the more than 14 million deaths of children under five years of age [*1*] occur during the neonatal period, with infections accounting for up to 70% of total mortality for this age group [2].

The organisms responsible for neonatal septicaemia vary across geographical boundaries and in time of onset. In addition, one organism or group of organisms may, over time, replace another as the leading cause of neonatal septicaemia in a particular region [*3*]. In Europe and North America, group B streptococci and *Escherichia coli* contribute to 70%–75% of cases of neonatal septicaemia [*4*]. The few epidemiological studies of neonatal septicaemia undertaken in the Middle East and in other developing countries [*5,6*] have shown important differences in the pattern and antibiotic susceptibility of pathogens compared with studies in European and North American countries [*7*]. Applying the results of these latter studies to developing country situations may not, therefore, be entirely appropriate. The local epidemiology of neonatal septicaemia should be constantly updated to detect changes in patterns of infection of pathogens and in their susceptibility to various antibiotics.

The aim of our study was to determine the local incidence of neonatal septicaemia at the main referral hospital in Al-Anbar governorate, Iraq, the most common bacterial pathogens associated with the disease and their antimicrobial susceptibilities.

Methods

The study was carried out over a 12-month period (March 2000–March 2001) at the neonatal care unit of the Maternity and Children's Hospital (MCH) in the city of Ramadi. MCH is the main referral hospital in Al-Anbar governorate. The unit admits newborns from the hospital's delivery room, postnatal ward and outpatients clinic, as well as referrals from other districts in the governorate. It has a capacity for 30 neonates, but occasionally admits in excess of this number, resulting in over-crowding. All newborns (that is, up to the first 28 days of life) admitted to the unit with signs and symptoms suggestive of septicaemia that were confirmed by a positive blood culture were enrolled in the study.

Blood samples of 1–2 mL for culture and sensitivity were taken from a peripheral vein using aseptic techniques. The skin was disinfected by applying tincture of iodine solution that was left to evaporate. The site was cleansed with a new sponge moistened with 70% alcohol solution, beginning at the centre and scrubbing in a circular motion outward. The samples were inoculated into a blood culture medium and sent directly to the laboratory where they were processed under the supervision of an expert microbiologist.

The culture medium used for primary isolation of the organisms was brain-heart infusion broth (DM 106: MAST Diagnostics, Bootle, United Kingdom) prepared by adding 1:10 (v/v) blood to media according to World Health Organization (WHO) recommendations [*8*]. MacConkey agar, SS agar and blood agar (DM 100: MAST Diagnostics, Bootle, United Kingdom) were used for subcultures. The blood culture bottles and inoculated plates were incubated at 37 °C. Antibiotic sensitivity testing was performed using the disc diffusion method with Mueller–Hilton II agar (BBL, Maryland, United States of America), as per the WHO-recommended Kirby–Bauer method [*8*]. Commercially available antibi-

otic discs (Oxoid, Basingstoke, United Kingdom) were used. After the sepsis investigations had been performed, each newborn suspected of having septicaemia received a combination of ampicillin (100 mg/kg) or ampicillin/cloxacillin (200 mg/kg) and gentamicin (5 mg/kg). This therapy was later modified according to culture and susceptibility results. Supportive measures were administered as indicated.

Results

During the study period, 1331 newborns were admitted to the MCH neonatal care unit. Of these, 118 (8.9%) were confirmed cases of neonatal septicaemia; 68 (58%) were males and 50 (42%) females, a ratio of 1.4:1. Of the septicaemic newborns, 78 (66%) were delivered at MCH, and 40 (34%) elsewhere. Thirty-three (33) neonates died, giving an overall mortality rate for the admitted patients of 28%. During the study period, there were 8451 live births at MCH; thus the incidence of neonatal septicaemia for babies born at this hospital was 9.2 per 1000 live births. There were 28 cases (24%) with early onset sepsis (less than 72 hours after birth), and 90 (76%) with late onset sepsis (over 72 hours after birth).

The most frequently isolated organisms were: *Staphylococcus aureus* (39% of cases), *Klebsiella pneumoniae* (30%), and *E. coli* (21%). These three organisms accounted for approximately 90% of all isolates. Details of other bacteria isolated and comparisons between the causative organisms of neonatal septicaemia cases delivered at MCH and those delivered elsewhere are presented in Table 1.

Table 1 Bacteriological profile of 118 neonates with positive blood culture for neonatal sepsis, comparing cases of late and early onset sepsis and those born within or outside the MCH

Organism	Total		Early onset sepsis		Late onset sepsis		Born at MCH		Born outside MCH	
	No.	%	No.	%	No.	%	No.	%	No.	%
Staphylococcus aureus	46	39	10	36	36	40	24	31	22	55
Klebsiella pneumoniae	35	30	6	21	29	32	31	40	4	10
Escherichia coli	25	21	10	36	15	17	20	26	5	13
Serratia species	4	3	1	4	3	3	2	3	2	5
Pseudomonas aeruginosa	2	2	–	–	2	2	–	–	2	5
Proteus species	2	2	–	–	2	2	–	–	2	5
Streptococcus pneumoniae	1	1	–	–	1	1	–	–	1	3
Neisseria meningitidis	1	1	–	–	1	1	–	–	1	3
Group B streptococci	1	1	–	4	–	–	1	1	–	–
Salmonella species	1	0.8	–	–	1	1.1	–	–	1	3
Total	118	100	28	100	90	100	78	100	40	100

MCH = Maternity and Children's Hospital in Ramadi, Iraq.

In newborns for whom *S. aureus* and *K. pneumonia* were the responsible pathogens, the majority of cases (36/46, 78%; 29/35, 83% respectively) were late onset. Together, these two pathogens were responsible for approximately 72% (65/90) of late onset cases, while *S. aureus* and *E. coli* contributed equally in early onset cases —10/28 (36%) each. Most cases of *Serratia* spp. (3/4, 75%) and all isolates of *Pseudomonas aeroginosa* and *Proteus* spp. were late onset (2/2), and the single isolate of Group B *Streptococcus* was early onset.

Among the tested antibiotics, cefotaxime, chloramphenicol and gentamicin were the most effective. They ranged in effectiveness, depending on the pathogen against which they were used, from 20%–34% of isolates susceptible; 40%–52%; and 37%–75%, respectively. The isolates exhibited a widespread resistance to most of the commonly used antibiotics in the neonatal care unit. Table 2 shows the different susceptibilities of bacterial isolates to the available antibiotic discs.

Discussion

The high frequency of neonatal septicaemia (8.9%) among neonates admitted to the neonatal care unit during the one-year study period is comparable with the reported figure of 9% from Saudi Arabia [*6,9*], indicating that sepsis is still an important cause of morbidity in this vulnerable age group. The incidence of neonatal septicaemia of 9.2 per 1000 live births at this hospital falls within the incidence of 5–20 per 1000 live births reported in several other countries [*5*].

Although a study from Saudi Arabia reported a much lower figure of 4.9 per 1000 live births [*7*], this variation is probably related to the difference in the prevalence of predisposing factors for neonatal septicaemia in the study population. In this study, there were more males than females, which is in line with the general concept of greater male susceptibility to infection [*10*]. The possibility of a sex-linked factor in host susceptibility has been suggested [*4*].

Table 2 **Antibiotic susceptibility profile: proportions of the major bacterial isolates that were susceptible to the antibiotics tested**

Antibiotic	*Staphylococcus aureus* (*n* = 46)		*Klebsiella* (*n* = 35)		*Escherichia coli* (*n* = 25)		*Serratia* (*n* = 4)	
	No.	%	No.	%	No.	%	No.	%
Benzylpenicillin	1	2	0	0	0	0	0	0
Cloxacillin	13	28	1	3	1	4	1	25
Ampicillin	13	28	5	14	3	12	0	0
Amoxicillin	4	9	3	9	2	8	0	0
Cephalothin	12	26	1	3	4	16	0	0
Cefotaxime	14	30	12	34	5	20	1	25
Chloramphenicol	23	50	14	40	13	52	2	50
Gentamicin	17	37	19	54	12	48	3	75

n = *total number of cases of infection with each organism.*

The overall mortality rate of neonatal septicaemia reported in the literature varies between 20%–75% [*11–13*]. The mortality rate of 28% in this study falls within this range, but is lower than figures reported from Saudi Arabia (44% and 38%) [*9,14*], Nigeria (31%) [*15*], and the United Kingdom (39%) [*16*]. It is possible that other factors, such as prematurity, congenital anomalies, birth asphyxia and meconium aspiration may contribute to death in septicaemic newborns. Differences in the prevalence of these factors may be responsible for the variability seen in mortality rates.

The three predominant isolates in our study were *S. aureus*, *K. pneumoniae* and *E. coli*. This pattern is similar to that observed in other developing countries (such as Saudi Arabia [*9,17*]). As the majority of cases in this study were of late onset and were delivered in a hospital, nosocomial infection is possible. Sources of infection might include mothers, other newborns, staff or equipment. Strict infection control protocols and regular surveillance of the neonatal care unit environment are necessary.

The lower incidence of group B streptococci revealed in our study is in agreement with reports from many developing countries [*5,6,9,17,18*]. By contrast, it is reportedly the most common isolate in more industrialized economies [*4*]. Differences in vaginal colonization between women in industrialized and developing countries are probably the reasons for this variation. In one study from Saudi Arabia, *S. aureus*, *K. pneumoniae* and *E. coli* accounted for approximately 60% of isolates in women who presented with vaginal discharge, while group B streptococci constituted only 5% of the isolates [*19*].

Among the tested antibiotics, the commonly isolated organisms showed a reasonable *in vitro* susceptibility to cefotaxime, gentamicin and chloramphenicol, but exhibited a very poor response to ampicillin and cloxacillin (commonly used antibiotics in this unit) and other antibiotics (Table 2). This widespread resistance can be attributed to the lack of facilities for culture and sensitivity, and of regular surveillance for antimicrobial susceptibilities, thus leading to indiscriminate and routine use of antibiotics in the neonatal care unit during the last decade (i.e. since the imposition of United Nations sanctions on Iraq in 1990). In view of the results of our study, a new approach, combining gentamicin with cefotaxime as a first-line therapy while awaiting culture and sensitivity results, is recommended. Although chloramphenicol was found to be relatively effective, its use is limited because of its serious toxicity (grey baby syndrome).

In conclusion, to optimize antimicrobial therapy, further studies to test a wider range of antibiotics such as ceftriaxon, ceftazidime, cefoxitin, piperacillin and amikacin are needed to understand the susceptibilities of the isolates to these antibiotics. Furthermore, in order to continually rationalize and refine antibiotic policy, our study highlights the importance of continuous surveillance of culture and sensitivity in the neonatal care unit environment, regular evaluation of local pathogens causing neonatal septicaemia and detection of any shift in their antimicrobial susceptibilities.

Acknowledgements

I would like to thank Mr Saleem O. Al-Mawla for his great help in microbiological investigations. I am also indebted to Dr Majeed Lafi, head of the Department of Pharmacology, and to Dr Fakhri J. Al-Dalla Ali, head of the Department of Paediatrics, for critical advice and comment.

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