

Aetiological agents, clinical features and outcome of septicaemia in infants in Ibadan

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Summary

The present study sought to determine the prevalence, clinical features and bacterial aetiological agents of septicaemia in post-neonatal infants (age 1–12 months) presenting with fever at the University College Hospital, Ibadan, Nigeria.

Study Setting: It was carried out at the Otunba Tunwase Children Emergency Ward (OTCHEW) (a 40 bedded ward) of the Department of Paediatrics, University College Hospital, Ibadan, Nigeria.

Patients: All postneonatal infants aged 1–12 months presenting with fever and who had not had antibiotic treatment in the week prior to presentation during the period June to November 1998 were enrolled in the study. Each child had a full clinical evaluation followed by a blood culture.

Results: The infants comprised 56 (54.9%) males and 46 (45.1%) females. The mean age was 5.6 (SD 0.3) months. The prevalence of septicaemia in the infants studied was 38.2%. Clinical features associated with increased risk of septicaemia among these infants were age ≤ 6 months, restlessness and a total white cell count $\geq 15000/\text{mm}^3$. The organisms isolated in the infants studied were *Escherichia coli* (35.9% of positive cultures), *Staphylococcus aureus* (33.3%), *Klebsiella* species (10.3%), *Streptococcus* species (7.7%), *Proteus* species (5.1%), *Pseudomonas* species (5.1%) and *Salmonella* species (2.6%). Mortality was significantly higher in patients with septicaemia (25.7% compared with those without septicaemia (7.9%).

Conclusions: Thirty eight percent of febrile infants presenting in this study had positive bacteria blood cultures, the most common organisms being *Escherichia coli* and *Staphylococcus aureus*. Few clinical features distinguished febrile infants with septicaemia from those without. It is recommended that febrile infants in our setting with clinical features associated with increased risk of septicaemia should be treated empirically with antibiotics since the probability of having septicaemia is significant.

Keywords: *Septicaemia, Infants, Nigeria, Clinical features.*

Résumé

Cet étude essaie de déterminer la fréquence, les traits cliniques et la cause étiologique bactérienne de la septicémie chez des enfants postnéonataux (âgés de 1 à 12 mois) atteints de la fièvre au Collège Hospitalo-Universitaire, Ibadan, Nigeria.

Cadre d'étude: Elle a été effectuée dans la Salle d'Urgence des enfants d'Otunba Tunwase. (OTCHEW) (la salle équipée 40 lits) du Département de la Pédiatriques, Collège Hospitalo-Universitaire, Ibadan, Nigeria.

Patients: Tous les enfants postnéonataux âgés de 1 à 12 mois

atteints de la fièvre et qui n'avaient pas eu le traitement antibiotiques le semaine précédente de présentation au cours de la période de juin au novembre 1998 se sont inscrit pour cet étude. Chaque enfant a subi une évaluation clinique rigoureuse suivi par la culture du sang.

Résultats: Les enfants sont: mâles 56 soit 54,9% et féminin 46 soit 45,1%. L'âge moyen était 5,6 (SD 0,3) mois. La fréquence de la septicémie chez les enfants étudiés était 38,2%. Les traits cliniques associés avec l'augmentation de risque de la septicémie parmi ces enfants étaient âgés ≤ 6 mois, agitation et le nombre total du globule blanc $\geq 15000/\text{mm}^3$. Les organismes isolés chez les enfants étudiés étaient *Escherichia coli* (35,9% de cultures positives), *Staphylocoques aureus* 33,3%, l'espèce *Klebsiella* 10,3%, l'espèce *Streptocoques* 7,7%, l'espèce *Proteus* 5,1%, l'espèce *Pseudomonas* 5,1% et l'espèce *Salmonellose* 23,7% par rapport aux ceux sans la septicémie 7,9%.

Conclusion: Trente huit pourcentage des enfants fébriles qui se présentent pour cet étude avaient des cultures du sang bactériens positifs. Les organismes les plus fréquents sont *Escherichia coli* et *staphylocoques aureus*. Peu de traits cliniques sont distingués chez des enfants fébriles atteints de la septicémie par rapport aux ceux sans la septicémie.

Nous proposons que des enfants fébriles dans notre cadre avec des traits cliniques associés avec l'augmentation de risque de la septicémie devront être traité empiriquement avec antibiotiques puisque la probabilité d'être atteint de la septicémie est innombrable.

Introduction

Septicaemia is an important cause of morbidity and mortality in children generally, and infants in particular^{1,2}. There has also been a substantial increase in the incidence of septicaemia during the last decade, particularly in developing countries³. The source of the infection varies, being more likely to be community-acquired in developing countries³⁻⁴ while hospital-acquired infections are more common in America and Europe⁵⁻⁶. Previous studies in USA and India⁷⁻⁹ have identified some risk factors for septicaemia and also suggested clinical features, which might predict septicaemia singly or in combination. However, septicaemia in children tends to present with non-specific clinical features and those clinical features found useful in one region may not necessarily apply to another region because of differences in disease epidemiology. Causative organisms also vary from place to place. For example, data from several studies in USA have shown that the most common causative organisms are *Streptococcus pneumoniae* (60-80%) and *Haemophilus influenzae* type b (20-30%)¹⁰⁻¹¹ while a study of Japanese children showed that *Staphylococcus aureus* (19.4%), *Pseudomonas* species (15.2%), *Escherichia coli* (12%), *Haemophilus influenzae* (11.4%)¹² are the major organisms responsible. Even within Africa, important differences exist with an East African study documenting *Salmonella typhi* (46%), *Streptococcus pneumoniae* (19%), *Salmonella enteritidis* (12%), *Salmonella*

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typhi (46%), *Streptococcus pneumoniae* (19%), *Salmonella enteritidis* (12%), *Salmonella typhimurium* (8%)¹³ in contrast to a study in Nigeria showing *Staphylococcus aureus* as the most common organism isolated (in 43% of the children studied)¹⁴.

Most studies of septicaemia in children have included children up to the age of 12 years. There are relatively few studies documenting aetiological agents of septicaemia in the first year of life with the exception of the neonatal period that has received very intense attention. In addition, it is known that significant shifts may occur in the pattern of causative organisms and in antimicrobial sensitivity even within the same community¹⁵. Against this background and in the absence of recent data in our environment, this study was undertaken to determine the prevalence of septicaemia in infancy, identify clinical features and determine the current aetiological agents of septicaemia in this age group.

Subjects and methods

This was a prospective study carried out at the Department of Paediatrics, University College Hospital (UCH), Ibadan, Nigeria. Ethical approval was obtained from the hospital ethical committee.

All infants aged 1 to 12 months presenting during the period June to November 1998 at the Otunba Tunwase Children's Emergency Ward (OTCHEW) of the Department of Paediatrics, University Collge Hospital (UCH), Ibadan, were evaluated for inclusion in the study. Eligible children were those who met the following criteria: (1) age 1 month to 12 months, (2) presenting complaint of fever with a rectal temperature of 38°C and above, (3) no antimicrobial treatment within the seven day period prior to presentation, and (4) no inherited disorder or congenital malformation that can increase the risk of infection (e.g. sickle cell anaemia and neural tube defects).

Infants meeting these criteria were identified on presentation and informed consent obtained from parent(s) or principal caregiver(s) to enrol them in the study. A full history was obtained from the parent(s) of each infant including presenting symptoms, a drug history and history of past illnesses. A clinical examination was then carried out and the temperature, weight, length, hydration status, clinical state, respiratory rate and pattern, heart rate, and presence of severe local infection were recorded. An initial clinical diagnosis was made after which 5 milliliters of venous blood was obtained aseptically from a peripheral vein for blood culture. Initial treatment was started after the blood culture was taken.

Two milliliters of the blood was inoculated aseptically into a glucose broth for detection of aerobic organisms. The blood cultures were incubated aerobically at 37°C for 7 to 10 days with subcultures made into blood agar, chocolate agar and MacConkey plates every day. Inoculated blood culture media were discarded as negative if there was no growth after continuous incubation for up to 7 to 10 days. The isolates were identified by standard methods¹⁶. When isolates were obtained, susceptibility to antimicrobial drugs was determined by the standardized disc diffusion method according to Stokes^{17,18}.

The remaining aliquot of blood was used for the estimation of packed cell volume, total white cell count with differentials, blood film for red cell and white cell morphology using standard methods. Thick blood films for malaria parasites were made and stained with 3% Giemsa stain at pH 7.2 and malaria parasites were identified under light microscopy. Where indicated, other cultures of body fluids such as pleural fluid, cerebrospinal fluid, urine were done. Chest radiographs were obtained when indicated.

An infant was judged to have septicaemia if there was growth of a known pathogen from the blood culture of an acutely ill, febrile child without a clinically apparent focus of infection.

Statistical analysis

All the clinical and laboratory data collected on each subject in the study were recorded on a standard proforma. The data were then entered using the Epi Info software package. Means of continuous variables were compared using Student's t-test. Categorical data were compared using Chi-squared test and Fisher's exact test where applicable. Differences were deemed to be statistically significant where $p < 0.05$.

Results

During the period of study 948 children were admitted into Otunba Tunwase Children's Emergency Ward (OTCHEW) of the University College Hospital, Ibadan. Of this number, 264 (27.8%) were postneonatal infants aged 1 month and above. Out of the 264 infants, 102 infants satisfied the criteria for inclusion in the study and were enrolled.

Clinical characteristics of subjects

The presenting clinical features in the study population are as shown in Table 1. Fever, which was an inclusion criterion, was present in all subjects. The most common symptoms were cough (52.9%), vomiting (45.1%), diarrhoea (33.3%), breathlessness (33.3%) and anorexia (30.4%). Nasal discharge, lethargy and convulsions occurred in 21.6%, 19.6%, and 19.6% respectively. The least frequent symptoms included rigors (4.9%), drowsiness (3.9%), septic spots (2.9%), eye discharge (2.9%), and grunting (1.9%).

The common signs were pallor (43.1%), hepatomegaly (41.1%) and splenomegaly (27.5%). Other signs were less common and included septic spots (13.7%), other skin lesions (12.7%), grunting (9.8%), abdominal distension (2.0%) and cy-

Table 1 Clinical features on presentation among the 102 infants in the study

Symptoms	No	% of total
Fever	102	100
Cough	54	52.9
Vomiting	46	45.1
Diarrhoea	34	33.3
Breathlessness	34	33.3
Anorexia	31	30.4
Nasal discharge	22	21.6
Lethargy	20	19.6
Convulsions	20	19.6
Excessive crying	18	17.6
Irritability	17	16.7
Skin lesions	12	11.8
Weakness	12	11.8
Restlessness	10	9.8
Rigors	5	4.9
Septic spots	3	2.9
Pallor	44	43.1
Hepatomegaly	42	41.1
Splenomegaly	28	27.5
Septic spots	14	13.7
Skin lesions	13	12.7
Grunting	10	9.8
Abdominal distension	2	2.0
Cyanosis	1	1.0

Table 2 Association of clinical features with septicaemia

Clinical feature	%(Septicaemic infants) n=39	% Non Septicaemic infants) n=63	Odds ratio (95%CI)	P value
Anorexia	33.3	28.6	1.25 (1.48,3.21)	0.384
Convulsions	17.9	20.6	1.74 (0.69,4.37)	0.474
Diarrhoea	41.0	28.6	1.74 (0.69,4.37)	0.140
Lethargy	28.6	14.3	2.36 (0.78,7.22)	0.072
Rigors	5.1	4.8	1.08 (0.09,9.90)	0.636
Restlessness	17.9	4.8	4.38 (0.91,27.7)	0.034*
Breathlessness	38.5	30.2	1.45 (0.57,3.63)	0.257
Excessive crying	23.1	14.3	1.80 (0.56,5.71)	0.192
Septic spots	2.6	3.2	0.80 (0.01,15.9)	0.674
Vomiting	48.7	42.9	1.27 (0.53,3.05)	0.354
Nasal discharge	20.5	22.2	0.90 (0.29,2.63)	0.521
Cough	53.8	52.4	1.06 (0.44,2.55)	0.524
Weakness	12.8	11.1	1.18 (0.27,4.70)	0.514
Irritability	25.6	11.1	2.76 (0.84,9.41)	0.05

$P < 0.05^*$

anosis (1.0%). The temperature of the subjects ranged from 38.0°C to 40.6°C with a mean of 38.5°C.

The mean age of patients with septicaemia and those without septicaemia were 4.6 (SD 2.4) months and 6.2 (SD 3.5) months respectively. There was statistically significant difference in their mean ages. ($t = 2.467$, $df = 1$, $p = 0.015$). The patients with septicaemia were younger than those without septicaemia. Age 6 months and less was significantly associated with septicaemia with 74.4% of infants being 1-6 months old compared to 25.6% of those > 6 months having septicaemia ($X^2 = 4.63$, $df = 1$, $p = 0.031$). Age less than 6 months was also associated with nearly a 3-fold increase in risk of septicaemia (OR = 2.78, 95% CI 1.09 – 7.53). The 39 patients with septicaemia had a male: female ratio 1:1.1 while the 63 patients without septicaemia comprised 37 male and 26 female with a male: female ratio of 1:0.7. (Odds ratio; 95% CI = 0.67 (0.28; 1.61): $p = 0.433$. There is no significant difference in the sex ratio of patients with and without septicaemia and thus gender was not a risk factor associated with septicaemia in these patients.

Table 2 shows the association of the presenting clinical features with septicaemia in the patients. There is no statistically significant difference in the means of the temperature on admission, respiratory rate, heart rate, liver and spleen sizes in patients with and those without septicaemia.

Septicaemia was confirmed in 39 infants out of the 102 subjects, giving a prevalence of 38.2%.

Table 3 Organisms isolated from blood cultures

Organism	No of patients n=39	% of positive cultures n=39	% of all cultures n=102
Escherichia coli	14	36	14
Staphylococcus aureus	13	33	13
Klebsiella species	4	10	4
Streptococcus species	3	8	3
Proteus species	2	5	2
Pseudomonas species	2	5	2
Salmonella species	1	3	1
	39	100	39

Bacterial aetiological agents of septicaemia

The pattern of bacterial isolates in the 39 positive blood cultures is shown in Table 3. Gram negative organisms, being the most common constituted (58.9%) of total positive cultures, with *Escherichia coli* being the most common single isolate found in (35.9%) of isolates. The other gram negative organisms were *Klebsiella species*, *Proteus species*, *Pseudomonas species* and *Salmonella species*. Only two gram positive organisms were isolated, these are *Staphylococcus aureus* and *Streptococcus species* in (33.3%) and (10.4%) of the positive blood cultures respectively.

Gram negative isolates were more common in the infants 4–6 compared with the 7–9 months old who had both types of organisms at almost equal frequencies. However, the organisms isolated in the 10–12 month old infants were gram negative. The age distribution of patients and type of organisms isolated are shown in Table 4

Out of the 39 patients that had septicaemia, 27 (69.2%) recovered, in 2 (5.1%) of them discharge was requested by the parents against medical advice and 10 (25.7%) died. For patients without septicaemia, 54 (85.3%) of them recovered, 4 of them (6.4%) were discharged against medical advice while 5 out of 63 of them (7.9%) died. Mortality was statistically significantly higher in patients with septicaemia (25.7%) compared with those without septicaemia (7.9%). ($X^2 = 4.69$, $df = 1$, $p = 0.030$). There was a 4-fold increase in mortality in patients with septicaemia compared with those without septicaemia. (OR = 4.0 95% confidence interval 1.1-16.13). Exclusion of patients discharged against medical advice did not alter the result. ($X^2 = 4.61$, $df = 1$, $p = 0.032$), (OR = 4.0 95% CI 1.1 - 16.22) Table 5 shows outcome in the studied infants.

Table 4 Age distribution of infants by type of bacteria

Age (months)	Gram-Positive n = 15 (%)	Gram-Negative n = 24 (%)
1-3(n=15)	5(33.3)	10(66.7)
4-6(n=14)	7(50.0)	7(50.0)
7-9(n=7)	3(42.9)	4(57.1)
10-12(n=3)	0(0.0)	3(100.0)

X^2 for linear trend = 0.184 $df = 1$ $p = 0.668$

Table 5 Outcome in patients with and without septicaemia

Outcome	Septicaemic Infants n=39 (%)		Non-Septicaemic Infants n=63 (%)	
	Recovered	27	(69.2)	54
Died	10	(25.7)	5	(7.9)
Discharged against Medical advice	2	(5.1)	4	(6.4)
Total	39	(100.0)	63	(100.0)

Discussion

Septicaemia still remained a very important cause of morbidity among infants who presented with fever at the University College Hospital, Ibadan. It occurred in 38.2% of patients enrolled into this study and 15% of all infants admitted into the Emergency Ward (OTCHEW) during the study period. This figure was much higher than those reported from United States of America with prevalence of septicaemia being between 3–10% from various reports¹⁹⁻²⁰. The higher prevalence observed in the study was however similar to previous works which showed that septicaemia was more common in tropical countries than in Europe¹⁹⁻²¹. One of the factors reported to be responsible for this is climate which encourages growth of certain organisms², this is in addition, to the fact that health care facilities are easily accessible and affordable in developed countries and as such children are presented to the hospitals early and promptly when they are febrile. However the findings in this study were in agreement with reports by Alausa et al²² who, working in the same hospital 23 years ago documented that 38.4% of all patients with septicaemia were infants, indicating that septicaemia was more common in infants than in older children. The male:female ratio of patients in this study was similar in those with and without septicaemia. This confirms previous reports that there is no sex preponderance in the incidence of septicaemia²².

A higher prevalence of gram negative organisms in this present study is in agreement with global trend²³⁻²⁴. In USA, gram negative organisms were isolated in 60% of patients²⁴, 66% of isolates documented in East Africa was also gram negative.¹³ The findings agree with those reported by Alausa et al²³ years ago from this same hospital²³. In the present study, gram negative organisms were more common in infants aged 1-3 months age group. This high prevalence of gram negative septicaemia in 1-3 months age group may be due to relative immaturity of their immune system and abnormal phagocytic functions²⁵. The study also showed that 33% of isolates in infants aged 1-3 months was gram positive and 50% of isolates in infants aged 4-6 months was also gram positive. Forty three percent of isolates in those aged 7-9 months was gram positive but there was none in those aged 7-12 months. This contrasts with findings by Akpede et al who reported that 52.5% of isolates in infants less than 6 months and 45.8% in those aged 6-12 months were gram positive³. The finding of only gram negative organisms in the infants aged 10-12 months may not be usual, however there is paucity of relevant data for comparison because of lack of documentation of aetiological agents in that narrow age range separate from other infants.

This present study confirms and extends the findings of

other workers that age is an important risk factor for septicaemia. Age ≤ 6 months was associated with a 3-fold increased risk of septicaemia, hence it shows that even within the narrow age range of infancy, age remains a strong risk factor for septicaemia. Teele et al²⁶ and Mc Gowan et al²⁷ found that an age of 24 months or less was the epidemiological factor with the highest sensitivity for septicaemia. Akpede et al³ working in Nigeria, also documented the highest prevalence of septicaemia in infants aged >1-12 months and the prevalence declined with age from 18.5% in the infants to 7% in older children.

Temperature was not found to be a predictor of septicaemia in this study which contrasts with previous findings by workers in USA like Teele et al²⁶ who found no positive blood cultures in children with temperatures < 38.9°C while 4.1% of those with temperature > 38.9°C had positive blood cultures, Mc Carthy et al²⁷ also documented positive blood cultures in 7.3% of children with temperature of 40°C. Their findings suggest that the risk of having septicaemia increases with increasing temperature and septicaemia was uncommon in children with temperature < 38.9°C. This study agrees with report by Akpede et al³ who documented that the prevalence of septicaemia was not influenced by temperature.

This study also confirms the fact that septicaemia is a significant cause of mortality with those with septicaemia having a mortality of 25.7% compared with 7.9% in those without septicaemia. This figure is higher than those documented by Lepage et al¹⁴ who reported a mortality rate of 9.3% in septicaemic patients in Rwanda and Akpede et al who reported 14.3% mortality³. The mortality figures in this study are lower than those reported by Alausa et al (38.4%)²². The difference in the mortality figures may be due to the fact that different causative organisms were implicated with varying degree of severity of the infection and complications.

A limitation of this study is that only cultures of aerobic organisms were undertaken; anaerobic culture was not done due to lack of facilities. Thus, the estimate of the prevalence of septicaemia in this study may be conservative. Also, it is uncertain how the inclusion of septicaemia due to anaerobic organisms may affect the findings of this study. However, this study still has clinical utility since most health facilities in our environment routinely undertake only aerobic cultures.

The following conclusions can be made from this study. Thirty eight percent of infants aged 1–12 months who presented at the Otunba Tunwase Children's Emergency Ward of the University College Hospital, Ibadan with fever (temperature $\geq 38^\circ\text{C}$) had septicaemia. The two most common organisms isolated were *Escherichia coli* and *Staphylococcus aureus*. Gram negative organisms were the most common as a group and only two gram positive organisms were isolated. Mortality was significantly higher in patients with septicaemia (25.7%) compared with those without septicaemia (7.9%). Therefore, every febrile infant, with or without localising signs, should have a blood culture done where possible.

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