

# Anaerobes in Neonatal Septicaemia: A Cause for Concern

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## Summary

The purpose of this study was to determine the prevalence and vertical transmission of anaerobic infection in early onset neonatal septicaemia in babies born to mothers with adverse perinatal factors.

One-hundred neonates born to mothers with one or more adverse perinatal factors were prospectively studied. Aerobic and anaerobic blood cultures were drawn in addition to rapid diagnostic tests. High vaginal swabs were also taken from all mothers prior to delivery.

Anaerobic *Clostridium* species infection was found in 5 per cent babies and all of them were symptomatic. Fifteen babies had aerobic infection. There was one baby with concomitant aerobic and anaerobic infection. There was no significant difference in sex distribution, birth weight, or gestational age between babies with aerobic and anaerobic infection. Similarly, there were no symptoms unique to anaerobic infection. None of the rapid diagnostic tests had a good sensitivity for anaerobic infection. Fifty-two per cent of the mothers had anaerobic growth in their vaginal swabs, but none had transmitted to their babies. All five babies recovered within 24–72 h of commencing therapy.

This study shows that anaerobes have a role in early onset neonatal septicaemia. They cause serious morbidity, but carry a good prognosis. For identification of such infection blood culture is mandatory.

## Introduction

Anaerobes as potential pathogens for neonatal sepsis have not been reported consistently till 1988 when observations over an 18-year period were published.<sup>1,2</sup> The incidence of anaerobic bacteraemia has been reported to be 1.8–2.5/1000 live births and anaerobe account for 13–26 per cent of all neonatal bacteraemia.<sup>1</sup> Do anaerobes form an important causative role in neonatal sepsis? This is an important question to answer in order to be able to institute appropriate therapy. This is especially true in situations where babies are born with adverse perinatal factors, and the clinical suspicion of sepsis is strong yet conventional aerobic cultures are negative or when organisms fail to respond to routinely used antibiotics. So far, indications and choice of antimicrobial drugs against anaerobes have been unclear. No prospective study in India has addressed this problem. Hence, this study was planned to evaluate the role of anaerobes in neonatal sepsis.

## Materials and Methods

One-hundred neonates born to mothers with at least one of the following risk factors were studied: prolonged rupture of membranes (PROM) more than 24 h, history of unclean vaginal examination (UVE), foul smelling liquor (FSL) and maternal fever  $\geq 38^{\circ}\text{C}$ . Babies who were asymptomatic at birth, but developed symptoms within the first 72 h of life were re-investigated. The following tests were done in all neonates: microESR, qualitative CRP, band count, absolute neutrophil count

(ANC), gastric aspirate (GA) for polymorphs, aerobic and anaerobic blood cultures. Micro ESR  $\geq 10$  mm at 1 h, band count of 20 per cent and  $> 5$  polys/HPF in gastric aspirate were taken as significant. ANC was interpreted from Manroe's chart.<sup>3</sup>

In addition to the usual aerobic blood culture, 3 ml blood was inoculated into PRAS bottle anaerobically. Anaerobic blood culture media contained brain heart infusion with cysteine hydrochloride, haemin, and menadione.

High vaginal swabs were also taken from mothers with the above-mentioned risk factors and cultured for anaerobes. Cotton-tipped sterilized swabs were used to collect secretions from mothers' vaginal fornix and transported in Robertson's cooked meat media for anaerobic processing. Subculture was done on anaerobic blood agar plates every 48 h for 3 weeks, incubated anaerobically at  $37^{\circ}\text{C}$  and any isolate was identified by standard methods.<sup>4,5</sup> Each anaerobic bacteria isolated was subjected to antibiotic susceptibility testing by modified Stokes' method.<sup>6</sup>

The neonates were categorized as follows:

- Definite sepsis—blood culture positive
- Probable sepsis—at least two rapid diagnostic tests positive in a symptomatic baby
- No sepsis—fulfilling neither of the above

## Results

Of the 100 babies studied, five had anaerobic septicemia and another 14 had aerobic septicemia (group A), 11 had probable sepsis (group B), and 70 were uninfected.

When compiling results the one case with simultaneous aerobic and anaerobic infection has been included in the 'anaerobic' group. The mean birth weights of babies with anaerobic and aerobic-infections were  $2170 \pm 463$  g and  $1915 \pm 783$  g, respectively. Their mean gestational ages were  $35 \pm 2.5$  weeks and  $34 \pm 4.3$  weeks, respectively. These observations revealed no significant difference in the two groups ( $P > 0.05$ ). Clinical data of the babies with anaerobic sepsis are shown in Table 1. One amongst them recovered without antibiotic therapy and, hence, probably had transient neonatal bacteraemia.

Results of the rapid diagnostic tests are shown in Table 2. None of these tests could individually predict anaerobic infection with good sensitivity, for identification of anaerobic infection. Therefore, blood culture was necessary.

All babies with anaerobic infection were symptomatic, whereas 12 out of 14 with aerobic growth had clinical symptoms. Respiratory distress was the commonest symptom in both groups. All the five babies with anaerobic infection had respiratory distress, two were lethargic, and one febrile. Other symptoms as present in aerobic infection were not present (Table 3).

Eighty-six mothers out of the 100 studied had received antibiotics. In 72 per cent of them infection had been prevented in the baby. Amongst the 14 babies whose mothers had not received antibiotics, three had aerobic

infection, two anaerobic and one probable sepsis. There were 73 isolates from 48 mothers. *Clostridium* was found in four cases in association with other anaerobes. However, there was no case of vertical transmission.

### Discussion

In spite of the growing awareness in anaerobes, routine anaerobic blood culture has not been asked for in neonatal septicaemia. The results of this study show that the role of anaerobes in neonatal septicaemia cannot be disregarded. The prevalence of anaerobic bacteraemia in babies born to mothers with adverse perinatal risk factors was 5 per cent. This accounted for 26 per cent of all the cases of proven sepsis. This is higher than that observed by Dunkle *et al.*<sup>7</sup> possibly due to our selection criteria. Sixty per cent of the babies with anaerobic infection were premature and the mean birth weight was  $2170 \pm 463$  g. These figures were similar to those in Noel and coworkers 18 year long study.<sup>2</sup> All babies with anaerobic infection were symptomatic against 12 out of 14 with aerobic infection. Hence, 29 per cent (five out of 17) of newborns with clinical disease and bacteraemia were infected with anaerobes. This is in comparison to 11 per cent in a previous study.<sup>7</sup> The probable reason for the high incidence of respiratory distress in our patients is possibly intrauterine aspiration of infected amniotic

TABLE 1  
*Different parameters in five babies with anaerobic infection*

No	Sex	Wt(g)	Gestation	Maternal antibiotics	Risk factors	Symptoms	Rapid diagnostic tests $\geq$ positive	Treatment	Outcome
1	M	2250	37	No	PROM, UVE	Respiratory distress, fever	Yes	C-penicillin Gentamicin	Well
2	M	2100	35 <sup>+2</sup>	Yes	PROM	Respiratory distress, lethargy	No	Nil	Well
3	M	2800	37	No	PROM, UVE	Respiratory distress, lethargy	Yes	C-penicillin Gentamicin	Well
4	F	2200	36	Yes	PROM	Respiratory distress	No	Cefotaxime Amikacin	Well
5	M	1500	31 <sup>+6</sup>	Yes	PROM	Respiratory distress	Yes	C-Penicillin Gentamicin	Well

TABLE 2  
*Distribution of rapid diagnostic tests in babies with infection and those without*

	n	Aerobes (n = 14)	Anaerobes (n = 5)	Probable infection (n = 11)	Non-infected (n = 70)
Raised micro ESR	16	5	1	4	6
CRP positive	24	11	2	6	5
ANC	32	8	2	5	17
Band count	17	1	2	6	8
GA for polys	9	1	0	5	3

TABLE 3  
*Distribution of symptoms in babies with and without infection*

Symptoms	Aerobes (n = 14)	Anaerobes (n = 5)	Non-infected (n = 70)
Respiratory distress	8 (57)	5 (100)	29 (41)
Lethargy	1 (7)	2 (40)	2 (4)
Hypothermia	2 (14)	0	1 (1.4)
Fever	0	1 (20)	2 (2.9)
Feed intolerance	1 (7)	0	5 (7)
Others:			
cyanosis	2 (14)	0	0
pallor	1 (7)	0	0
polycythemia	0	0	1 (1.4)
petechiae	0	0	2 (2.9)
abdominal distension	1 (7)	0	1 (1.4)

Percentage values given in parentheses.

fluid. In other words, babies with anaerobic infection born to mothers with suspected chorio-amnionitis are more likely to present with respiratory distress. It is possible that anaerobes in neonates cause minor bacteraemia, hence other serious symptoms were not encountered. Of the 23 neonates studied by Chow *et al.*,<sup>1</sup> 65 per cent had maternal history of premature rupture of membranes (PROM) and 52 per cent had foul smelling liquor (FSL). We had no case with FSL. All five babies with anaerobic infection were born to mothers with PROM. This was probably because PROM was the commonest risk factor in our study group. These risk factors were also present in those with aerobic infection so an association with anaerobic infection could not be established.

Four cases out of the five with anaerobic sepsis had pure isolate of *Clostridium* sp. in 21 days subculture and in one there was concomitant *E. coli* infection. None of these babies had underlying cord infection or gut perforation which predisposes to clostridial sepsis. None of them had typical features of clostridial infection like jaundice, haemolysis, haemoglobinuria as have been described earlier in one neonate.<sup>8</sup> This might be due to prompt institution of appropriate therapy or these were of non-histotoxic strains.

Fifty-two per cent of the maternal swabs were positive for anaerobes. Anaerobes are not very common commensals of the genital tract in antenatal women near term.<sup>9,10</sup> Amongst them, *Clostridium* is rare. Only four out of 73 isolates in our study were Clostridia. There was no case with vertical transmission. One such case has been reported so far in the literature.<sup>8</sup> Hence, the organisms isolated from the neonates were either acquired *in utero* or from the lower genital tract where faecal contamination is not uncommon.

In spite of being very sick at admission, all the babies with anaerobic sepsis recovered within 24–72 h. All of them received treatment except one. In the one case where no treatment was offered sepsis screen was negative and symptoms subsided within 24 h age. The infection, therefore, seems to have been self-limited and at least in one case there was spontaneous clearance of the organism.

Our conclusion, therefore, is that while anaerobes cause symptomatic infection, such infection is transient and possibly could remit without intervention. For practical purposes, however, an empiric therapy has to be given so as not to leave the 5 per cent cases without treatment. Since rapid diagnostic tests have shown poor sensitivity in this study we would conclude that nothing short of a properly-taken blood culture can identify this group of babies especially in mothers with adverse perinatal factors.

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