

# Evaluation of Risk Factors and Supportive Investigations in the Diagnosis of Neonatal Sepsis

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This prospective study was conducted in the Department of Pediatrics of King Edward Medical College and Mayo Hospital Lahore from September 1999 to April 2000. Risk factors, blood culture along with clinical features and certain hematological parameters pointing towards the diagnosis of sepsis were studied. LBW (39%) and PROM (31%) were the most important risk factors. The blood culture was positive in 78(52.7%) cases and common pathogens isolated were Klebsiella 33(42% of all positive cases), Staphylococcus aureus 13(16.6%) and E. Coli 16(20.5%). In culture negative cases diagnostic efficacy of risk factors, clinical features and certain haematological parameters were evaluated. Clinical features most commonly associated were lethargy 41(93% of all culture negative cases), poor feeding 39(88.6%), respiratory distress 18(40%) and hypothermia 12(27%). In the same group abnormal TLC was (<5000 or >20000 in 34%), where as mini-ESR (>15mm in 58%), CRP(>8 in 84%) and I/T ratio(> 0.2 in 77%) was significantly raised. Thus in culture negative patients combination of risk factors along with above mentioned hematological parameters may be useful in diagnosis.

**Key words:** EOS - early onset sepsis, LOS - Late onset sepsis

Incidence of neonatal sepsis in developed countries is 1-4/1000 live births<sup>1</sup> where as in Pakistan it is reported to be 1.13-3.8/1000 live birth, in different studies. The high mortality & morbidity of NNS<sup>2,3</sup>, coupled with vague symptoms of the syndrome necessitates an early and accurate diagnosis. The backbone of the diagnosis is positive blood culture. which is taken as gold standard<sup>4</sup>. Ironically yield of blood culture is generally low<sup>5</sup>. Since signs and symptoms of disease is also non-specific, we have to rely on surrogate markers of disease. There is dire need indeed to find out epidemiological predictors or supportive investigations, which can guide us reliably in early diagnosis of NNS. It has been found that certain lab investigations, in combination, not in isolation give a reliable diagnosis of NNS. They are:

1. Abnormal TLC (Total leukocyte count <5000/mm<sup>3</sup> or > 20000/mm<sup>3</sup>).
2. Immature/mature neutrophil ratio > 0.2
3. Mini ESR >15 mm in first hour.
4. CRP level >8 mg.

These tests on blood can easily be done & easily available in the absence of gold standard blood culture. They can prove a reliable substitute for early diagnosis of NNS.

## Objectives

1. To study perinatal risk factors and clinical features pointing towards the diagnosis of sepsis in newborns( Asses the predictive value of history and clinical features).
2. To assess usefulness of laboratory predictors in the diagnosis of neonatal sepsis.

## Patients and methods

The prospective study was conducted in Department of Pediatrics, Mayo hospital Lahore over a period of 8

months from September 1999 to April 2000. Cases with suspicion of sepsis were included in the study. Depending upon time of presentation, patients were classified EOS or LOS, according to standard criteria<sup>(1)</sup>. Only those cases were enrolled in the study who were free of congenital anomalies and had not received antibiotics before admission. Both full term, LBW and premature babies were included. History and examination findings were recorded on a pre-designed performa with special emphasis on selected perinatal risk factors associated with NNS. List of factors include in performa (Table 1).

Table 1. Clinical and Laboratory data evaluated

Risk factors	Sign & symptoms	Lab investigations
PROM, with duration >18 hours.	Poor feeding	Abnormal TLC
Chorioamnionitis.	Lethargy	Immature to mature neutrophil ratio (I/T)
Mode of delivery	Hypothermia	
Home/Hospital delivery, SVD or C-Sec.	Fever	Mini-ESR>15mm 1 <sup>st</sup> hr
Dia handling before delivery	Fits	CRP
Gender of baby	Respiratory distress	Blood C/S
Premature or LBW baby	Sclerema Vomiting	CSF culture in suspected cases

The diagnosis of NNS was made on the clinical features combined with lab data. The gold standard of NNS was positive blood culture. An effort was made to correlate perinatal risk factors & supportive lab investigations with confirmed cases of NNS. If the blood culture was negative, but clinical features were suggestive of septicemia,



correlation was made between perinatal risk factors and supportive lab investigations to see the predictive value of two for confirmation of diagnosis. Based on these parameters cases were classified as

**Proven cases:** defined as patients with positive blood culture.

**Probable cases:** defined as patients with negative blood cultures but clinical features suggestive of NNS with supportive investigations.

**Less likely case:** negative blood culture and normal supportive investigations.

**Results**

This study was conducted over a period of eight months. During this period 148 neonates were admitted with suspicion of neonatal sepsis. Ninety-six (64.8%) had early onset sepsis where as 52(35.2%) had late onset sepsis. Mean age of the neonates in this study came out to be 6.43 days. Neonatal sepsis was twice more common in boys.

**Figure 1: Sex distribution in cases of neonatal Sepsis.**



79% of these babies were full term as compared to 21% LBW and premature babies. Nearly half (54%) of the deliveries took place at hospitals, all the rest were conducted by traditional birth attendants ('dais') at home.

We also looked at predisposing risk factors for sepsis (Table 2). Low birth weight (LBW) and premature rupture of membranes (PROM) for more 18 hour duration were found to be most significant factors seen in 39% and 31% cases respectively.

**Table 2: Risk factors for neonatal sepsis (n=148).**

Risk factors	Positive %
PROM > 18 hrs.	31%
Maternal fever	09%
Chorioamnionitis	04%
LBW & Premature	39%
Prolonged / difficult labor	19%

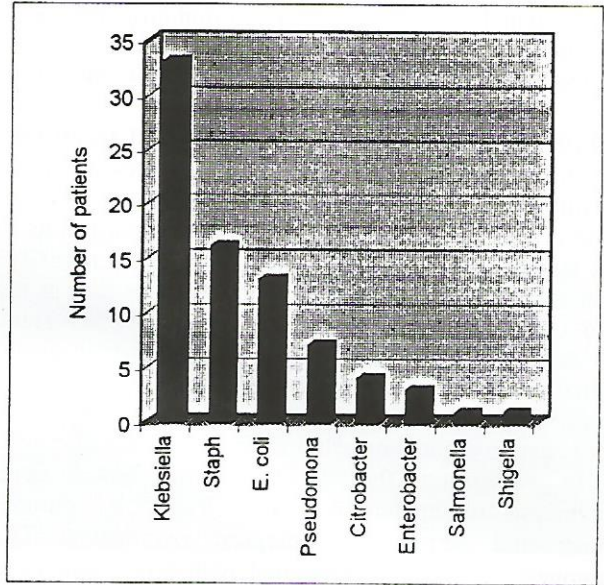
Based on the results of blood culture the data on three categories of our study patients (Table 2).

**Table 3: Classification of the study population.**

Category	No. of Cases
Proven cases	78 (52.7%)
Probable cases	44 (29.7)
Less likely	26 (17.6)

Figure 2 shows different organisms grown on blood culture. Klebsiella was the most common organism grown (42%) followed by Staphylococcus aureus (21%) and E coli (17%).

**Fig. 2. Pathogenic organisms obtained on culture report**



In the probable cases of neonatal sepsis with negative blood culture report, important clinical features are enumerated in table 4.

**Table 4 Clinical features in Probable cases (n=44).**

Clinical feature	Number(%)
Lethargy	41(93.1%)
Poor feeding	39(88.6%)
Respiratory distress	18 (40.9%)
Hypothermia	12 (27.3%)
Fever	4 (9.1%)
Fits	4 (9.1%)
Sclerema	4 (9.1%)
Vomiting	10 (22%)

The results of supportive investigations in different groups are shown in Table 5.

**Table 5: Supportive investigations.**

Group	E.S.R.	C.R.P.	Abnormal T.L.C.	I/T Ratio
Proven (n=78)	48 (61%)	67 (86%)	30 (38%)	69 (88%)
Probable (n=44)	26 (58%)	37 (84%)	15 (34%)	34 (77%)
Less likely(26)	0	06 (23%)	05 (19%)	04 (15%)

**Discussion**

Sepsis is an important cause of neonatal deaths in Pakistan<sup>2</sup>. These babies tend to have overwhelming bacteremia with poor localization of infections into any particular organ<sup>1,4</sup>. Hence the clinical manifestations are



nonspecific and vague. Its early diagnosis demands high index of suspicion. In developing countries where health care facilities are scarce blood cultures are often not available or yield is low<sup>5</sup>. Most of the time one has to rely on clinical features and adjunct investigations<sup>6</sup>. This study is an effort to assess predictability of non microbiological features, which may be helpful in formulating a working principle in areas with minimal facilities.

Out of 148 cases of neonatal sepsis, only 78(52.2%) were culture positive (Klebsiella) 33(42.2%), Staphylococcus aureus 13(16.6%) and E. Coli 16(20.5%), confirming the established fact that neonates are more susceptible to gram-negative infections. There was no isolate of GBS in this study. This confirms the results of other studies from Pakistan<sup>7</sup> which have shown that GBS is not an important pathogen in NNS in this part of the world unlike the developed countries. In another study from Lahore<sup>8</sup> culture positivity was reported 40% and Klebsiella as the most common organism. At the same time data agrees with the conventional concept of enteric gram negative organisms being the commonest<sup>1</sup>.

In remaining the diagnosis was based upon combination of epidemiological risk factors, clinical features and certain hematological parameters. The commonest risk factors associated with septicemia were prematurity & LBW (39%) and history of PROM of duration >18 hours. In only 4 % the cases chorio-amnionitis was present. These findings are in consonance with the standard literature<sup>1</sup>. Diagnostic efficacy of clinical features also was evaluated in our study, lethargy(93%), poor feeding (88.6%) were significantly more common compared to Hameed's data<sup>8</sup>. It may be so because of lower socioeconomic level of the patients in our catchments area and tendency to present late. Although lethargy, poor feeding, respiratory distress are classically present in most of the cases but it is striking observation that 64% of these cases had normal body temperature. The other hematological parameters which served as surrogate markers in suspected cases were in order of significance Increased CRP (84%), ESR (51%), I/T ratio (>0.2) in 77% and abnormal TLC (34 %).

The raised level of CRP appears to be one of the most significant marker and there is evidence that more utilization of this test may reduce unnecessary antibiotic exposure and shorten hospital stay in neonates<sup>10</sup>. In Hameed's study<sup>8</sup> from Lahore I / T ratio was reported 38% which is much lower as compared to our data (77%). Abnormal leukocyte count<sup>11</sup> was the least impressive variation in our study (34%) which is in agreement with the Hameed's data (20%). Mini-ESR appears to be another useful diagnostic tool in diagnosis of NNS, especially when used in combination. This supports the concept that

clinical data combined with very simple tests could be a very good predictor of sepsis in a suspected case<sup>13,14,15</sup>. This will not only be cost effective but at the same time will improve the outcome due to early diagnosis if a panel of such investigations is routinely used in our neonatal care units. Since a combination of these investigations have high sensitivity and specificity it is justified to use broad spectrum antibiotics in neonates suspected of having sepsis till we receive culture report.

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