

INDICATORS OF EARLY OUTCOME IN NEONATAL SEPSIS

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The purpose of this study was to evaluate different parameters predicting outcome of neonatal sepsis. It was carried out at the neonatal unit of Ghurki Trust Teaching Hospital, Lahore from February 2004 to May 2005. This was an analytical comparative study performed prospectively. A total of 100 culture proven cases of neonatal sepsis were included. Complete data including birth weight and time interval between onset of symptoms and arrival at hospital was recorded. Complete blood counts and arterial blood gas analysis were performed in all cases. Overall mortality was 37%. Among the total of 100 cases 51% (n=51) were low birth weight (LBW) while 49% (n=49) were of normal birth weight, 40.7% (n=24) expired from LBW group, while 26.5% (n=13) from those with normal birth weight. Mortality was higher ($P<0.05$) in LBW babies. Among them 29.03% (n=18) expired from those who reached within 24 hrs of onset of symptoms (n=62) whereas 50% (n=19) expired from those who reached after 24 hrs (n=38). This difference was also significant ($P<0.05$). Hypothermia affected 39% of the cases. Mortality was significantly higher ($P<0.05$) in cases who developed hypothermia. Among laboratory parameters, leukopaenia, thrombocytopaenia, and acidosis were individually associated with high mortality ($P<0.05$), while leukocytosis was not significantly ($P>0.05$) associated with neonatal mortality. It was concluded that neonatal sepsis has high mortality. Some of the clinical and laboratory parameters are useful to recognize high-risk cases. Early referral can reduce mortality. Long-term follow-up of the survivors is indicated.

Keywords: Neonatal sepsis, Outcome, Indicators.

INTRODUCTION

Neonatal sepsis is a common cause of neonatal morbidity and mortality with an annual incidence of 2-6/1000 live births in the developed countries of the world¹. In the developing countries, the estimated incidence is 3-4 times higher and neonatal sepsis remains one of the most common reasons for admission in neonatal units². This is mainly due to lack of health education, poor antenatal care and lack of trained staff to conduct deliveries. The association between maternal urinary tract infection, pyrexia, vaginal discharge and unclean vaginal examination during labour and development of early onset neonatal sepsis is well established³.

In the developing countries like Pakistan, the higher incidence leads to increased morbidity and mortality due to neonatal sepsis. According to a community and facility based data, neonatal sepsis has significant contribution to the perinatal and neonatal mortality rates⁴. The hospital based data also indicate that 30-37% of neonatal deaths are due to sepsis in the neonatal units^{5,6}. The higher

proportion of low-birth-weight (LBW) deliveries (up to 25%), places these infants susceptible to sepsis and its related mortality³. Another factor contributing to high mortality is delay in reaching of the sick newborns at hospital, in our setup⁷.

To reduce the incidence and mortality due to sepsis, prevention of LBW deliveries, good maternity services, early recognition of high risk cases and prompt referral are needed^{4,8}. A lot of work is being done for early recognition, rapid diagnosis and outcome-based categorization of the cases of neonatal septicaemia. Although the precise prediction of outcome in terms of morbidity and mortality is difficult, some of the indicators are very useful. Both clinical and laboratory parameters can be used for this purpose⁹.

Regarding clinical indicators, LBW babies, late onset sepsis, temperature instability, development of seizures and delay in arrival at hospital are usually considered to be associated with bad prognosis¹⁰⁻¹². Laboratory parameters associated with high mortality include abnormal leukocyte

counts, increased I:T ratio (immature to total leukocytes counts ratio), severe neutropenia, deranged renal parameters, thrombocytopenia and severe metabolic acidosis¹³⁻¹⁵. In the past, both of these groups of parameters have been proved useful in the early detection of neonatal sepsis, when used in different combinations. Currently, their role as prognostic indicators is also being evaluated^{13,16}.

In our community the resources and services for advanced laboratory work up are inadequate. In such circumstances, these simple indicators can help in early recognition and prompt referral of the high-risk cases of neonatal sepsis. In the neonatal Intensive Care Units, prevention and early recognition and appropriate management of these clinical and laboratory parameters can help to reduce neonatal morbidity and mortality.

MATERIALS AND METHODS

Study Population

A total of 100 culture proven cases of neonatal sepsis admitted to neonatal unit at Ghurki Trust Teaching Hospital, Lahore, were studied. The study was performed from February 2004 to May 2005. It was an analytical comparative study conducted in a prospective manner. Age range was 0-28 days. Neonates admitted with clinical features of sepsis, and proven on blood culture were included.

METHODS

A complete data including antenatal, natal and postnatal events, birth weight, risk factors for sepsis, and time interval between onset of symptoms and arrival at hospital were recorded. A thorough examination was performed. Blood samples were collected for complete blood counts and blood cultures before starting any antimicrobial therapy. During the hospitalization, arterial blood gas analysis was monitored in all cases. Serum electrolytes, renal parameters, CSF examination and culture; and urine culture were performed when indicated. Along with that, clinical manifestations including temperature instability were recorded. Hypothermia was defined as body temperature $\leq 97^{\circ}\text{F}$ of at least 20 minutes duration. Platelets counts of $<100 \times 10^9/\text{L}$ was taken as thrombocytopenia. Total leukocyte counts $> 20 \times 10^9/\text{L}$ were taken as leukocytosis while $< 5.0 \times 10^9/\text{L}$ as leukopenia. $\text{pH} < 7.35$ was labeled as severe acidosis. Statistical analysis was done by applying Chi-square test to obtain P-Value.

RESULTS

The overall mortality was 37% (n=37), as shown in Fig-1. Among these 51% (n=51) cases were LBW, while 49% (n=49) were having normal birth weight i.e. $\geq 2.5\text{kg}$. Twenty four patients (40.7%) expired from LBW group while 13 (26.5%) expired from those having normal birth weight [Table 1]. This difference was statistically significant ($P < 0.05$). Among these 62% of the cases (n=62) reached hospital within 24 hours after onset of symptoms, while 38% (n=38) reached after 24 hours. The mortality was significantly high ($P < 0.05$) in the cases that took > 24 hours in reaching hospital [Table 2].

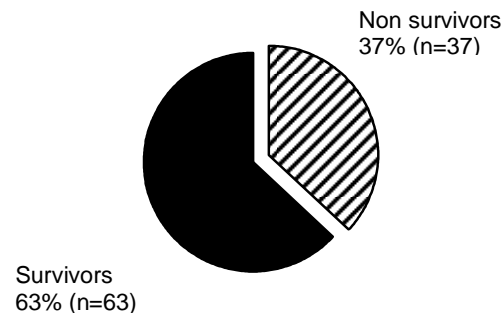


Fig. 1: Distribution of Cases on The Basis of Mortality.

Table 1: Association between birth weight and mortality.

| Sr. No. | Birth Weight | No. of Cases | Expired | Survived |
|---------|---------------|--------------|-------------|-------------|
| 1 | < 2.5 kg | 51 | 24 (47.05%) | 27 (52.94%) |
| 2 | ≥ 2.5 kg | 49 | 13 (26.53%) | 36 (73.46%) |

($P < 0.05$)

Thirty nine percent of the total cases developed hypothermia and 23 (58.9%) expired from this group. Sixty one percent of cases didn't develop hypothermia and 14 (22.9%) expired from this group. Hypothermia was significantly related to high mortality ($P < 0.05$) [Table 3]. Similarly, leukopenia, thrombocytopenia and severe acidosis were significantly associated ($P < 0.05$) with high mortality when analyzed individually in relation to mortality. Leukocytosis, on the other hand was not a significant parameter ($P > 0.05$) in determining mortality [Table 4].

Table 2: Association between mortality and time-lapse between onset of symptoms and arrival at hospital.

| Sr. No. | Time Interval | No. of Cases | Expired | Survived |
|---------|---------------|--------------|-------------|-------------|
| 1 | < 24 Hours | 62 | 18 (29.03%) | 44 (70.93%) |
| 2 | > 24 Hours | 38 | 19 (50%) | 19 (50%) |

(P < 0.05)

Table 3: Relationship between hypothermia and outcome.

| Sr. No. | Hypothermia | No. of Cases | Expired | Survived |
|---------|-------------|--------------|-------------|-------------|
| 1 | Present | 39 | 23 (58.97%) | 16 (41.02%) |
| 2 | Absent | 61 | 14 (22.95%) | 47 (77.04%) |

(P < 0.05)

Table 4: Association between laboratory parameters and outcome.

| Sr. No. | Laboratory Parameters | Survivors (n=63) | Non Survivors (n=37) | P. Value |
|---------|-----------------------|------------------|----------------------|----------|
| 1 | Leukocytosis | 18 | 15 | > 0.05 |
| 2 | Leukopenia | 14 | 17 | < 0.05 |
| 3 | Thrombocytopenia | 18 | 19 | < .05 |
| 4 | Acidosis | 20 | 20 | < 0.05 |

DISCUSSION

More than 5 million neonatal deaths occur worldwide every year, accounting for two-thirds of deaths of children under one year of age⁴. Pakistan is among the countries having highest neonatal mortality rate⁽¹⁷⁾. Neonatal sepsis remains one of the major causes contributing to this high mortality rate. It accounts for a significant number of admissions in the neonatal units and is also responsible for 30-37% of neonatal deaths in the hospitals⁶.

Our results have shown a mortality of 37%, which is in accordance with other data from different parts of the country^{4,8,18}. Low birth weight babies constituted 51% of our study population, indicating high prevalence of risk factors for LBW / premature deliveries like poor antenatal services, inadequate birth intervals and maternal under-nutrition, in the community surrounding our hospital. The mortality was significantly high in LBW infants as compared to

neonates having normal birth weight. This is supported by studies from Karachi¹⁵, Islamabad⁵ and Lahore⁶. The time interval between onset of symptoms and start of management plays a significant role in determining outcome, as indicated by our analysis. In a community based analysis of "delay in reaching hospital", it was found that economical and socio-cultural factors, illiteracy and delayed referral are the main causes in our country¹⁹.

Mortality was higher in the cases that developed hypothermia, in our results. The cold injury due to hypothermia can lead to formation of ice crystals between and within cells, disturbing the functions of all body systems. The hypothermia in neonatal age has not only found to be associated with high neonatal mortality but also been associated with poor psychomotor development on long term follow up of survivors of neonatal sepsis^{10, 11}.

Regarding laboratory parameters, we found that leukopaenia is significantly related to high mortality ($P < 0.05$), while leukocytosis is not a significant factor in determining mortality ($P > 0.05$). In the past, abnormal total leukocyte counts (TLC) alone or in combination with I:T (immature to total leukocytes count ratio) had been used for early detection of neonatal sepsis^{(16),(20)}. It has now been found that these parameters can also help in predicting the outcome of sepsis¹³. Some of the workers have also established association between low Absolute Neutrophil Counts (ANC) and worse outcome in neonatal sepsis²¹. Our finding of thrombocytopaenia as an indicator of high mortality is supported by other data¹⁴. Clinical evidence of thrombocytopaenia in the form of bleeding tendency in neonates has also been found to be associated with worse outcome¹⁵.

We found that acidosis is also an outcome determining parameter and high mortality was seen in neonates having severe acidosis on arterial blood gas analysis. A scoring system for predicting neonatal outcome, named as SNAP (Score for Neonatal Acute Physiology), also supports that acidosis is associated with high mortality in neonatal sepsis²¹.

It has been **concluded** from this study that neonatal sepsis is a serious illness associated with high mortality in our country. Early referral and prompt management of high risk cases can help in improving outcome. Some of the clinical and laboratory parameters are very useful in predicting the outcome. Further work is needed to analyse these and some others parameters as predictors of morbidity by monitoring long term sequelae of the condition.

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