DISCUSSION
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The early diagnosis of neonatal septicemia is primarily based on clinical evaluation of the case. Many babies are treated with several days of antibiotics because of possible infection while waiting for bacteriologic culture.

The present study was conducted over a period of one year (July 1992 to September 1993) in the Department of Paediatrics and Department of Microbiology, M.L.B. Medical College, Jhansi. This study was designed to evaluate certain rapid diagnostic tests to detect neonatal septicemia at an early stage. Statistical evaluation of tests was done in terms of sensitivity, specificity, positive predictive accuracy and negative predictive accuracy. Simultaneously, a clinico-bacteriological profile of neonatal septicemia was drawn.

The potential value of rapid diagnostic tests is to exclude infection when uncertainty exists about the clinical diagnosis.

As depicted in Table No. 1, seventy five cases of suspected neonatal septicemia were included in the
present study. Cases were classified into Category 'A' (Bacteriologically positive); Category 'B' (Bacteriologically negative); Category 'C' (healthy neonates). The results of diagnostic test obtained in Category A and Category B neonates were compared.

In view of the observations depicted in tables I to XII, following inferences were drawn:

Table II shows that out of 35 cases in Category A, 15 (42.9%) were premature babies, while only 27.5% prematures were present in Category B. Thus prematures constituted a sizeable proportion of case who had bacteriologically proven septicemia. Chandna et al (1988) studied cases of neonatal septicemia in order to establish an early diagnosis in such cases. Authors reported that 36% cases of neonatal septicemia in their study were prematures. However, Saxena et al (1978) observed prematurity in only 21% of such cases. A significantly higher incidence of septicemia in premature infants is probably due to the lack of inherent defensive mechanism in them, both, at cellular and humoral level. It may, as well be due to relatively longer stay and excessive exposure of premature babies to diagnostic and supportive procedure in the hospital.

Regarding the birth weight of study material, it was found that more than half of the cases were low
birth weight. It is depicted in table III that 57.3% of the babies in Category A were low birth weight and 37.5% of babies in Category B were low birth weight. These findings are in agreement with the observation of Benuck et al (1983) and Philips et al (1980) who reported 62% and 63% low birth weight babies in their study which was done to evaluate the diagnostic test for rapid diagnosis of neonatal septicemia.

Low birth weight infants, both premature and full term, have low IgG and are more susceptible to infection. While placental transport of IgG from maternal to fetal circulation increases with the maturity, this transport is hampered in small-for-date infants who are often the product of placental insufficiency (Chandna et al, 1988).

That neonatal septicemia is more often observed in male babies, is a well documented fact. The observed range of male predominance is 59 to 82% (Somu et al, 1978). As depicted in table IV, 71.4% cases in Category A were male babies and Category B included 80% of male babies. This percentage of male preponderance is in agreement with the observation of Khatua et al (1980), Placzek et al (1983) and Philips et al (1980), who observed 70.7%, 70% and 61% male predominance respectively in their study of neonatal septicemia.
The higher incidence of males, as observed in the present study and those of others, could be explained on the basis that factors regulating synthesis of gamma globulin is probably situated on 'X' chromosomes. Presence of one X chromosome in the male infant confers less immunological protection to him as compared to female infants. Another factor of male preponderance is that males are better cared for than females, in our society.

Apart from prematurity and low birth weight a number of perinatal adverse factors are counted as high risk factors in neonatal septicemia viz. leaking per vagina, meconium staining and birth asphyxia. There is no generally accepted definition of premature rupture of membranes. Huston et al (1961) included in their study all cases in whom membranes had ruptured one hour or more before the onset of labour. A common convention is to regard premature rupture of membranes when it occurs 24 hours or more before delivery. In the present study, cases were selected with the history of rupture of membranes 7 12 hour before the delivery as has been done by Mishra et al (1989) and Manroe et al (1977). In the present study, majority of cases (65%) of neonatal septicemia had a history of leaking per vagina 712 hour before the delivery (table V). These findings are comparable with the observation of Mishra et al (1989) and Anand et al (1991) who observed 68.9% and 33.5% cases
of neonatal septicemia respectively with history of premature rupture of membranes. However, Habel et al (1972) and Boyd et al (1978), in a study designed to establish early identification of sepsis in infants with respiratory distress, observed little relation between the premature rupture of membranes and development of neonatal septicemia. The result of present study, however, indicated that prophylactic administration of antibiotics to infants delivered after prolonged rupture of membranes was, perhaps, necessary and potentially safer.

HEMATOLOGICAL TEST

(a) **White Blood Cell count (Table VI)** :

In the past changes in white blood cell parameters, among neonates, were regarded least useful for the diagnosis of septicemia, since these values were thought to be too erratic. Recently Xanthou et al (1972) studied changes in White Blood Cells (WBC) more precisely, in healthy and diseased neonates, in order to establish their usefulness to support the diagnosis of neonatal septicemia.

In the present study emphasis was placed on the total WBC count, since white blood cells constitute the first line of defence. Leucopenia of \( < 5000 \) cells/cu mm was observed in 65.7% of Category A cases in the present
study and 17.5% in Category B cases. These values correlate closely with the findings of Singh et al (1987) who observed leucopenia in 65.5% of proven sepsis cases. However, Chandna et al (1988), Mishra et al (1989) and Namdeo et al (1985) observed very low percentage of cases with leucopenia, 12%, 39% and 40% respectively in proven cases of septicemia and 11.5% and 13% respectively in probable sepsis cases.

Observations of severe leucopenia are not altogether surprising, in view of the short half life of leucocyte, only 6-7 hours, due to massive removal of injured cells, probably, by the lungs (Boggs, 1967). Though the neonates are at a disadvantage, due to poorly developed immune response, they do respond to infective insult like an older child (Gregory et al, 1972). During an acute infection neutrophils are rapidly released from the neutrophilic storage compartment (NSC) into circulation, which manifests as neutrophilia (both mature and band form) and leucocytosis and provide potent cells for migration to infected tissues (Christensen et al, 1980). Simultaneously the neutotic and maturation compartments proliferate to replenish neutrophilic storage compartment. It appears that Neutrophilic storage compartment replacement had failed to keep pace with Neutrophilic storage compartment exit either due to marrow failure or increased sequestration (Xanthou et al, 1972).
An altogether different mechanism, excessive neutrophil margination can result in an indistinguishable blood picture of neutropenia, but the neutrophil proliferative pool and neutrophil storage compartment remains normal and the host's neutrophil supply is not compromised (Christensen et al, 1980).

(b) **Band Cell Count and Band/Neutrophil ratio (B/N ratio)**

*(Tables VII and VIII)*

The leucocyte count and differential leucocyte count provide a useful diagnostic tool to diagnose neonatal septicemia. However, extreme variability in leucocyte count of neonates has led to skepticism regarding its value as a diagnostic tool (Haider, 1972). Hence, the differential count is required to determine the absolute value of the various cell types and the immature cells especially 'Band Cells'. Moreover, Band to neutrophil cell ratio is given more stress since it is found to be more sensitive as an index to diagnose neonatal septicemia (Christensen et al, 1978).

The present study was carried out to assess the value of neutrophil and Band cell counts as the early indicators of septicemia. In the present study it was observed that Band cell count 710% was present in 74.5% of Category A cases and in 45% of Category B cases. Various other workers have also reported similar high...
Band Cell counts in cases of neonatal septicemia. Parida et al (1980), Mishra et al (1989) and Xanthou et al (1972) reported 50%, 80% and 88% cases respectively having Band cell count \( \geq 10\% \) in cases of neonatal septicemia.

Likewise Band/Neutrophil ratio \( \sqrt{0.2} \) (B/N ratio) in the present study was observed in 77% of Category A cases and 45% of Category B cases. These results are in agreement with the observation of Namdeo et al (1985), Philips et al (1980) and Mishra et al (1989) who reported B/N ratio \( \sqrt{0.2} \) in 84%, 90% and 91% cases, respectively, in neonatal septicemia.

During bacterial infection, increased number of neutrophils are released from the bone marrow into the blood, thereby providing cells necessary for accelerated neutrophil migration into infected tissues (Marsh et al, 1967). This increase in neutrophil supply from the marrow and the resultant changes in blood leucocyte 'numbers' and 'types' appears to be essential for host resistance to bacterial infection (Christensen et al, 1980). As neutrophils are released from the marrow, more and more immature non-segmented cells (Band cells) reach the blood, a process inferred to as a 'left shift' (Wintrobe, 1976). These findings have been found to be valuable adjunct to the early diagnosis of bacterial infection (Akensua et al, 1976). This 'shift to left' is quantified by using Band/Neutrophil ratio \( \sqrt{0.2} \) in the present study.
(c) *Micro Erythrocytic Sedimentation Rate (mESR)*

*(table IX)*:

The observed values of micro ESR, a simple, inexpensive test requiring only few drops of capillary blood, are depicted in Table X. As is evident from table IX, elevated level of mESR (7-8 mm in 1st hour) was present in 77.1% Category A cases and in 22.5% Category B cases. These findings of mESR in neonatal septicemia confirm the observation of Parida et al (1980), Namdeo et al (1985) and Singh et al (1986) who reported elevated values in 71.4%, 80% and 74% cases respectively in proven cases of neonatal septicemia.

Erythrocytic sedimentation rate is a non-specific indicator of tissue damage and is known to be elevated in infective states. The rate of increase is dependent upon the severity of morbid process. (Wintrobe, 1976).

**Bacteriological profile (table X):**

The 'Gold Standard' for a definite diagnosis of septicemia remains "the isolation of micro-organisms from blood culture". Various workers have reported positivity of blood culture in suspected cases of neonatal septicemia ranging from 30% - 70%. In the present study, 46.6% of positivity was achieved. Namdeo et al (1985), Chandra et al (1983) and Guha et al (1978) reported positivity
of blood culture in 50%, 48% and 40% cases respectively. Relatively high positivity was reported by Mittal et al (1980) 60% and Mehrotra et al (1985) 60%. Whereas Bhakoo et al (1975) and Choudhary et al (1975) found positivity of 32% and 30.6% respectively. This relative low incidence of bacterial isolation in their study could be explained on the basis of clinical over-assessment of newborns or could be owing to excessive use of antibiotics before admission in the hospital.

Regarding the micro-organism isolates in the present study, staphylococcus aureus was the top scorer with positivity of 37%. Similarly, Somu et al (1978), Saxena et al (1980), Mishra et al (1985) reported staphylococcus aureus as the commonest organism in neonatal septicemia cases. E.coli and Pseudomonas aeruginosa were the next common isolates in the present study, with positivity of 28.5% and 17.1% respectively. Bhakoo et al (1968), Chaudhary et al (1975), Guha et al (1978) in their observation of bacterial isolate confirmed the findings of present study regarding E.coli, being next most common isolate. However, Singh et al (1987) and Chaturvedi et al (1989) reported Klebsiella as the commonest isolate, in their studies on neonatal septicemia.

Regarding the recent emergence of Staphylococcus aureus as the commonest isolate in neonatal septicemia...
Ayengar et al (1991) and Chaudhary et al (1975) opined that handling of the baby by unclean hands, poor sterilization, delivery and follow-up in unclean environment are some of the factors which increase the incidence of staphylococcus aureus infection.

Clinical Manifestation (table XI):

Non-specific, vague and subtle clinical features of neonatal septicemia mimicking several other conditions like birth asphyxia, hypoglycemia, hypothermia and intracranial hemorrhage make the task of diagnosing neonatal septicemia very difficult.

As evident from the table XI, lethargy, poor feeding and hyporeflexia seen in 88.5%, 85.7% and 83.7% respectively, were the most common presenting feature of Category A cases. While these features were present in only 78%, 72.3% & 67.3% cases respectively, of Category B septicemia. Likewise, Khatua et al (1986) reported refusal of feeds in 92.3% cases and lethargy in 74% cases of neonatal septicemia. Chandna et al (1988) reported lethargy in 70% cases and hyporeflexia in 66% cases and very low incidence of refusal of feed in 46% cases of neonatal septicemia.

Fever was observed in 62.6% cases in the present study. However, Mishra et al (1989), Chandna et al (1988) and Khatua et al (1986) reported very low
incidence of fever - 9%, 14% and 24% respectively in cases of neonatal septicemia.

Omphalitis, hepatomegaly, abdominal distension and jaundice were present in about 50% of cases in the present study. Whereas, Mishra et al (1989), Chandna et al (1988) observed very low incidence of omphalitis, abdominal distension and jaundice ranging from 5% to 16%.

Sclerema, associated with very high mortality, has been seen in 31.4% cases in the present study. Findings of the present study are comparable to the findings of Mishra et al (1989) who observed 38% cases of sclerema in their study. Contrary to the present study Chandna et al (1988) observed sclerema in only 10% cases.

Khatua et al (1986) reported that refusal of feeds, lethargy, diarrhoea, hypothermia, abdominal distension, jaundice were the most common early clinical features. Respiratory distress, apnoic spells, convulsions and sclerema were the late features and were associated with the poor prognosis in cases of neonatal septicemia.

**Sensitivity, Specificity, Positive Predictive Accuracy and Negative Predictive Accuracy (table XII)**

The accuracy in making an early diagnosis depends on the sensitivity and specificity of the test employed. In earlier studies (Philips et al, 1980; Squire et al, 1982)
done so far, sensitivity and specificity of the test was determined from the probable cases of sepsis (negative blood culture) having one or more abnormal diagnostic test, thus lending a bias in favour of the screening tests employed. As these probable cases (negative blood culture) can not be strictly considered cases as control. Because moreover there may be some technical mistakes in doing blood culture or the baby may have received antibiotics prior to drawing blood for culture.

In the present study standard negatives taken from controls were used to determine the statistical parameters as was done by Singh et al (1987) for diagnosis of neonatal septicemia.

In table XII are depicted statistical values regarding the sensitivity (ability of the test to diagnose the disease), specificity (ability of the test to exclude the non-diseased cases), positive predictive accuracy and negative predictive accuracy of the rapid diagnostic test to detect early cases of neonatal septicemia.

In the present study it was observed that Band/Neutrophil ratio \( \geq 0.2 \) and micro Erythrocytic sedimentation rate \( \geq 8 \text{ mm in 1st hour} \) were equally and most sensitive parameters for the diagnosis of cases of septicemia. Both achieved the sensitivity index of 77%.
These observations are comparable to the findings of Chandna et al (1988) and Singh et al (1987) who observed that Band/Neutrophil ratio $7/0.2$ had 67% and 68% sensitivity index respectively. Mishra et al (1989) and Philips et al (1980) however reported sensitivity index for B/N ratio of 92% and 96% respectively.

Statistical calculations were done to find out the specificity of various hematological test done, in the present study. It was observed that Band/Neutrophil ratio $7/0.2$ achieved the maximum specificity of 96%. These findings are in close agreement with the findings of Singh et al (1987) who observed specificity of 81%.

Contrary to the findings of the present study, Chandna et al (1988) observed very low specificity of 31% for Band/Neutrophil ratio test.

Maximum positive predictive accuracy in the present study for Band/Neutrophil ratio $7/0.2$ was again the highest (table XII), 96.4% which is comparable to the findings of Mishra et al (1989) who observed positive predictive accuracy of Band/Neutrophil ratio $7/0.2$ to be 73%. However, Philips et al (1980) and Chandna et al (1988) reported positive predictive accuracy of Band/Neutrophil ratio $7/0.2$, 26% and 47% respectively.

Band/Neutrophil ratio $7/0.2$ was also found to have maximum negative predictive accuracy 75%, among all
the four diagnostic tests. This observation from the present study was in close agreement with the findings of Mishra et al (1989) who observed negative predictive accuracy of 94% of Band/Neutrophil ratio.

On analysing all four diagnostic test, it was observed that Band/Neutrophil ratio /0.2, in case of neonatal septicemia, had the maximum sensitivity, specificity, positive predictive accuracy and negative predictive accuracy.

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