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Letter to Editor

Paediatrics Section

Letter to Editor: Utility of Sepsis Screen in the Early Diagnosis of Neonatal Sepsis

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Keywords: Absolute neutrophil count, Clinical sepsis, Sample size

We read with great interest the original article by Bhale CP et al., [1] in the recent issue of your journal. At first, we would like to commend the authors for their endeavour but at the same time would like to make the following comments, clarification to which would benefit the general readers of the journal:

Query 1. Sensitivity and specificity of a diagnostic test depends on the pre-test probability of the condition under consideration [2]. In an attempt to find the utility of sepsis screen, the authors compared the gold standard diagnosis of neonatal sepsis with neonates having culture negative clinical sepsis. But they did not mention the criteria used to define clinical sepsis in the study. This is of particular interest as all the parameters were found to be significantly different in the culture positive cases compared to culture negative clinical sepsis. In this context, one very important aspect of sepsis screen in the management of neonatal sepsis needs to be highlighted. The purpose of the sepsis screen is mostly to rule out sepsis rather than to rule in sepsis. The clinician at the very beginning must classify a newborn into either of the groups with 'high probability of sepsis' and 'low probability of sepsis' based on standard risk factors and clinical assessment [3]. The role of sepsis screen in the first group is questionable as they are advised to be started on antibiotics irrespective of the results of the screen after sending blood culture; especially in low resource settings with high rates of neonatal sepsis and mortality. It is the group of newborn with low probability of sepsis who benefit from sepsis screen, as two negative sepsis screens reassures the treating physician in withholding antibiotics [3].

Query 2. The authors provide no information on sample size calculation; it is very important as sample size would influence the precision and power of the study [4].

Query 3. It is not mentioned whether informed consent was obtained from the parents/ guardians of the neonates for inclusion in the study.

Query 4. It is not clear why the authors chose to separately collect sample for micro ESR by heel prick while sample for other blood investigations were also being taken from the same patients.

Query 5. [Table/Fig-1] divides the newborns based upon place of delivery into groups of 'inside NICU' and 'outside'. We wonder whether the authors wanted to actually denote the place of acquiring the infection or the place where the babies were cared for instead of place of delivery.

Sex	Male (%)	Female (%)
	54 (59.3)	37 (40.7)
Birth weight	<2.5 kg	≥2.5 kg
	74 (81.3)	17 (18.7)
Gestational age	<37 weeks	≥37 weeks
	60 (65.9)	31 (34.1)
Age of onset	≤3 days	>3 days
	58 (63.7)	33(36.3)
Place of delivery	Inside NICU	Outside
	48 (52.7)	43 (47.3)

[Table/Fig-1]: The distribution of cases in culture positive group [1].

Query 6. An Absolute Neutrophil Count (ANC) <1800/mm^3 was considered as abnormal for all the neonates irrespective of the gestation. But ANC is known to vary depending on the gestational age and post natal age. Therefore, it is recommended that the cut off for ANC should be as per Manroe's chart for term and Mouzinho's chart for preterm infants [5]. This could have also contributed to the very low sensitivity of ANC observed in the present study.

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Reply from the Author

Answer for Query 1: Inclusion criteria: The neonates admitted to NICU of our institute were included in the study. The clinical criteria used to define sepsis were: the neonates presenting with one or more clinical features listed below—

- Hypothermia or fever
- Lethargy, poor cry, refusal to suck
- Hypotonia, absent neonatal reflexes
- Vomiting, diarrhoea, abdominal distension
- Bleeding, petechie, purpura
- Skin changes: multiple pustules, abscess, sclerema, mottling, umbilical discharge and redness
- Bradycardia or tachycardia
- Bulging anterior fontanelle, blank look, high pitched cry, excessive irritability, not arousable, comatose
- Respiratory distress, grunt, apnoea, gasping respiration
- Neonates with septicemia having one or more risk factors like prematurity, low birth weight, birth asphyxia, foul smelling liquor amnii, unclean per vaginal examination before delivery, prolonged rupture of membranes and prolonged labour.

Exclusion criteria

- Neonates with major congenital anomalies
- Neonates who received antibiotics before admission.

The study constitutes of the samples taken only at a single time, therefore the sample could be obtained before starting the antibiotics in a " high probability of sepsis" group.

Answer for Query 2: The sample size was calculated using following formula [1]

$$Ss = \frac{Z^2 \times p(1-p)}{d^2}$$

where:— Z= Z value(1.96 for 95% confidence interval)

p= expected proportion in the population based on pilot studies or previous studies (12% in our institute)

d= absolute error (5%) minimum sample size by using above formula is 162. Our sample size was 191.

Answer for Query 3: Institutional Ethical Committee Clearance was taken prior to the study. Informed consents were obtained from the parents of the neonates.

Answer for Query 4: Shah Y et al., stated that ESR values determined on blood obtained by heel stick and collected directly in Natelson capillary tubes were correlated with ESR values determined simultaneously by Wintrobe's method on venous blood [2].

Vinay BS et al., also used the same method in a recent hospital based study [3].

Answer for Query 5: We had included the samples of the neonates admitted to the NICU of our institute in the present study. The term "outside" was used to denote the babies born outside the institute and admitted to NICU of our institute. The term "inside" was used to denote the babies born in our institute and admitted to NICU of our institute.

Answer for Query 6: As correctly quoted above and observed is the reason of the low sensitivity of Absolute Neutrophil Count. That is why the use of Sepsis Screen instead of single criterion was recommended in the study.

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Regards

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