



A STUDY OF FEVER IN NEW BORN AND ASSOCIATION WITH SEPSIS

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ABSTRACT Sepsis is a clinical syndrome characterised by signs and symptoms of infection with accompanying bacteraemia. Many newborn present with complain of fever in daily OPD. The aims and objective of present study was to evaluate fever in newborn and its association with sepsis.

METHODS: This is a prospective observational study conducted in the neonatology department of Smt. Shardaben Municipal General Hospital during the period of January 2009 to November 2010. Total 44 neonates from 1st hour of life to 28th day of life were included in this study.

RESULTS: 44 neonates were enrolled in the study group who had an axillary temperature of more than or equal to 100.4°F, out of which 26 (59.09%) were male and 18 (40.90%) were female. From 44 neonates 18 (40.90%) had sepsis out of which 10 (22.72%) neonates had proven sepsis with positive blood culture. According to present study most common presentation of neonatal sepsis in neonates along with fever is refusal to feed (45.8%). Out of 44 neonates, 10 (55.5%) have blood culture positive and 8 (44.44%) have blood culture negative. C reactive protein is positive in 17 (38.63%) neonates and negative in 27 (61.37%) neonates. Out of 44 neonates 6 (13.63%) have total count <5000 and 2 (4.54%) have total count >15000. I:T ratio is <0.2 in 16 (36.36%) neonates and >0.2 in 18 (63.63%) neonates.

CONCLUSIONS: Fever is commonly associated with sepsis. All effort should be made to rule out sepsis in newborn who present with fever, maintain the warm chain, detect fever early and take prompt measure to correct it.

KEYWORDS : fever, sepsis, new born, blood culture, c reactive protein

INTRODUCTION

Fever in new born is an emergency sign of systemic infections mostly of bacterial infections [16]. The incidence of serious bacterial infections ranges from 4-28% [2, 15, 21]. Neonatal sepsis is 2nd most common cause of neonatal mortality in India [11]. Sepsis is a clinical syndrome characterised by signs and symptoms of infection with accompanying bacteraemia. It encompasses various systemic infection of the infant such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infection. Superficial infections are not usually included under neonatal sepsis. Sepsis in newborn present with feature such as temperature instability, refusal to feed, excessive irritability, lethargy, convulsion, frequency of stool, difficulty in breathing etc. As rise in body temperature is commonly associated manifestation of sepsis, any newborn who present with fever should be promptly investigated for sepsis and should be treated. The objective of present study was to study fever and its association with sepsis.

METHODS

It was prospective observational study conducted at NICU of Smt. Shardaben Municipal General Hospital, affiliated to N.H.L. medical College, Ahmedabad. The study period was from January 2009 to November 2010. Total of 44 new born from 1st hour life to 28th day of life with axillary temperature >100.4°F were included in this study. The standard digital thermometer must be left for 3-5 minutes in the axilla for correct assessment of body temperature. While taking temperature in axilla, take care to direct the tip of the thermometer towards the apex of the axilla. For a digital thermometer, wipe the area extending with 70% isopropyl alcohol before and after each use.

INCLUSION CRITERIA:

- All babies from 1st hour of life to 28th day of life regardless of gestational age with axillary temperature >100.4°F were included.

EXCLUSION CRITERIA:

- Neonates with major congenital malformations and neonates with severe birth asphyxia.

A detailed history was taken regarding gestational age, gender, birth

weight and weight on admission, maternal age and parity, mode of delivery, maternal illness and drug intake. Blood sampling was done with proper aseptic precaution. Investigations like complete blood count, haemoglobin, C reactive protein and CSF analysis were done as needed to rule out sepsis.

OBSERVATION

Total 44 patients were taken irrespective of age, sex and gestational age.

TABLE 1: Comparative studies showing demographic characteristic.

Characteristic	Present study	Shah HH et al[9]	Janakiraman D et al[7]
Sex			
Male	26 (59.09%)	56%	60%
Female	18 (40.90%)	44%	40%

As such there is no sex preference in present study. Total 44 out of which 26 (59.09%) were male and 18 (40.90%) were female which is a reflection of normal population sex ratio which is 930 female per 1000 male.

TABLE 2: Comparative studies showing gestational age wise distribution.

Gestational age	Present study	Janakiraman D et al[7]
Full term	39(88.63%)	87%
Pre term	5(11.37%)	13%

Total 44 out of which 39 (88.63%) were full term and 5 (11.37%) were pre term. This table suggests that fever is more common presentation with full term because full term infants have better thermal regulation.

TABLE 3: Comparative studies showing symptoms

SYMPTOMS	Present study	Urvashi Rana et al[24]	Chudgar HH et al[19]	Shah CP et al[22]	Janakiraman D et al[7]
Fever	44(100%)	59.76%	44%	30%	100%
Refusal to feed	33(45.8%)	77.84%	84%	80%	-

Difficulty in breathing	15(20.83%)	-	-	-	32%
Icterus	9(12.5%)	33.81%	-	40%	8%
Convulsion	6(8.3%)	44.89%	-	30%	8%
Frequency of stool	5(9.94%)	37.90%	13%	10%	10%
Cyanosis	3(4.16%)	24.78%	15%	-	-
Lethargy	1(1.3%)	68.80%	42%	-	48%

According to this table fever is associated commonly with refusal to feed 33 (45.8%) which is followed by difficulty in breathing 15 (20.83%), icterus 9 (12.5%), convulsion 6 (8.3%), frequency of stool 5 (6.94%), cyanosis 3 (4.16%) and lethargy 1 (1.3%). Difficulty in breathing was observed in 15 (20.83%) of patient. It may be due to respiratory cause such as pneumonia, pneumothorax, meningitis, ICH, metabolic acidosis or severe abdominal distension due to sepsis. Present study comparable to 77.84% Urvashi Rana et al [24], 84% Chudgar HH et al[19], 80% Shah CP et al[22] shows fever most commonly associated with refused to feed. According to Janakiraman et al [7] fever is most commonly associated with lethargy.

TABLE 4: Comparative studies showing culture positivity rate

	Present study	Janakiraman D et al[7]	Urvashi Rana et al[24]	NNPD 20002-03[18]	Tallur et al[23]	Joshi et al[24]	Roy et al[16]
Blood culture positive	55.5%	12%	52.61%	28.6%	64.8%	25%	47.50%
Blood culture negative	44.44%	88%	47.39%	71.4%	37.2%	75%	52.5%

The blood culture positive cases were classified as proven sepsis. Out of total 44 patient 18 (40.90%) patient had septicemia in which 10 (55.5%) patients had positive blood culture report which is proved sepsis and 8 (44.5%) patients were considering as sepsis with help of septic screen, other laboratory investigation, clinical sign and symptom. Result of present study co-related to Vora et al [25], Urvashi Rana et al [24] and Maayan-Metzger et al [16] and culture proven sepsis is 10%, 47.18%, 7.40% respectively.

Present study was comparable with the studies conducted by Janakiraman D et al [7], NNPD 20002-03[18], Tallur et al [23], Joshi et al [14], Roy et al [16] [19] and showed a very low culture positivity. It may be due to sampling error, stage of bacteraemia or previous treatment with antibiotics.

TABLE 5: Comparative studies showing complete blood count

Complete Blood Count	Present study	Janakiraman D et al[7]
Total count		
<5000	6(13.63%)	9%
5000-15000	36(81.81%)	62%
>15000	2(4.54%)	29%
IT Ratio		
<0.2	16(36.36%)	-
>0.2	18(63.63%)	-
C reactive protein		
Positive	17(38.63%)	44%
Negative	27(61.37%)	88%

According to present study from 44 neonates total count was <5000 in 6 (13.63%) neonates and >15000 in 2 (4.54%) other neonates had total count within normal limit. According to EMA total count <4000 and >20,000 is significant. Out of 44 neonates 18 (63.63%) have IT ratio >0.2 which is significant.

Table 6: Study Association between C reactive protein and Blood culture report

CRP Positive (17)(38.6%)		CRP Negative (27)(61.4%)	
Blood culture positive	Blood culture negative	Blood culture positive	Blood culture negative
10(22.7%)	7(15.9%)	0(0%)	27(61.4%)

Out of 44 new born, 10 had both CRP and blood culture report positive and 7 patients had CRP positive and blood culture negative. This may be due to false positive result of CRP or it may be due to error in collection in blood culture and sensitivity sampling, stage of disease or previous treatment with antibiotic.

DISCUSSION

Neonatal sepsis is a major public health problem having high incidence and mortality in developing countries. About 0.75 million neonates die every year in India, the highest for any country in the world [13]. There is remarkable heterogeneity among studies regarding the case definition of neonatal sepsis. The presence of a positive blood culture historically constitutes the “gold standard” for the presence of neonatal sepsis [26].

EOS is defined as onset of sepsis in the first 3 day and is mostly the result of vertical transmission of bacteria from mothers to infants during the intrapartum period [1]. LOS is defined as infection occurring after 1 week of life and is attributed to the horizontal transmission of pathogens acquired post natal and is more insidious in onset [4].

Clinical signs and laboratory signs (presence of at least two clinical symptoms and at least two laboratory signs) associated with neonatal sepsis according to the report on the expert meeting on neonatal and paediatric sepsis of EMA (2010)[12].

- Clinical signs are modified body temperature: core temperature greater than 38.5 °C or less than 36 °C and/or temperature instability Cardiovascular instability: bradycardia (mean HR less than the 10th percentile for age in the absence of external vagal stimulus, beta-blockers or congenital heart disease) or tachycardia (mean heart greater than 2 SD above normal for age in the absence of external stimulus, chronic drugs and painful stimuli) and/or rhythm instability, reduced urinary output (less than 1 mL/kg/h), hypotension (mean arterial pressure less than the 5th percentile for age), mottled skin, impaired peripheral perfusion Skin and subcutaneous lesions: petechial rash, sclerema Respiratory instability: apnoea episodes or tachypnea episodes (mean respiratory rate (RR) over 2 SD above normal for age) or increased oxygen requirements or requirement for ventilation support Gastrointestinal: feeding intolerance, poor sucking, abdominal distention Non-specific: irritability, lethargy and hypotonia.
- Laboratory signs are White blood cells (WBC) count: <4,000 x10⁹ cells/l OR >20,000 x10⁹ cells/l Immature to total neutrophil ratio (I/T) >0.2 Platelet count <100,000 x10⁹ cells/L C reactive protein > 15 mg/L OR procalcitonin ≥ 2 ng/ml (The cut-off for procalcitonin in neonatal sepsis has not been clearly defined, as the currently available published data are still controversial). Glucose intolerance confirmed at least 2 times: hyperglycaemia (blood glucose >180 mg/dL or 10 mMol/L) OR hypoglycaemia (glycaemia < 45 mg/dL or 2.5 mMol/L) Metabolic acidosis: Base excess (BE) <-10 mEq/L OR Serum lactate > 2 mMol/L

Low WBC and absolute neutrophil counts, as well as high immature-to-total neutrophil ratio (I:T) are associated with an increased risk of infection [10]. A large number of studies have been performed to evaluate the use of complete blood count (CBC), differential count, and immature to total leukocyte ratio (I:T) for the diagnosis of neonatal sepsis. Although the CBC has a poor predictive value, serial normal values can be used to enhance the prediction that bacterial sepsis is not present [6,20]. A total leukocyte count of <5000 to 7500/mm³ can be used to infer the diagnosis of neonatal sepsis [8]. CRP is an acute phase reactant synthesized by the liver. It has a half- life of 24–48 h. It takes 10–12 h for CRP to change significantly after the onset of infection. Serial determination of CRP 24–48 h after the onset of symptoms increases its sensitivity. Serial CRP measurements may also be helpful in monitoring the response to treatment in infected neonates and thus may help clinicians guide the duration of antibiotic therapy. Fever in neonates may occur due to secretion of pyretic inflammatory cytokines which raises the hypothalamic temperature, as well lead to elevated body temperature [17]. Non-infectious conditions being associated with fever in new born includes dehydration, breast-feeding, high birth weight, and caesarean section [5,25].

CONCLUSION

According to present study incidence of sepsis in patient with fever is high. All effort should be made to rule out sepsis in newborn who present with complain of fever. Maintain hydration, keep babies in thermo neutral environment and with help of early clinical suspicion and septic screen we can start treatment early for sepsis while blood culture report is awaited.

ABBREVIATION

EOS-early onset septicaemia
 LOS-late onset septicaemia
 HR-heart rate
 RR-respiratory rate
 CRP-c reactive protein
 NICU-neonatal intensive care unit
 F-Fahrenheit
 CSF-cerebrospinal fluid
 ICH-intracranial haemorrhage
 WBC-white blood cell
 CBC-complete blood count
 OPD-out-patient department

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