**INTRODUCTION**

Neonatal sepsis is defined as the presence of positive bacterial cultures in blood, cerebrospinal fluid and or urine associated with systemic clinical signs of infection such as fever, temperature instability, irritability, poor feeding and respiratory distress.\(^1\) Neonatal sepsis is the most common cause of neonatal mortality. It is responsible for 30-40% of neonatal deaths in developing countries.\(^2\) The incidence of sepsis is 3 per thousand live...
births according to national neonatal perinatal database. 
According to World health organization (WHO) estimates, there are about 5 million neonatal deaths a year, with 98% occurring in developing countries. The epidemiology of neonatal sepsis in developing and developed countries shows some important differences in pattern of etiological agents and their antibiotic susceptibilities. More ever epidemiology within a geographical area may also be different, highlighting the need for surveillance of neonatal sepsis in various regions for optimal therapy.

Neonatal sepsis can be divided into early onset sepsis (EOS) or late onset sepsis (LOS) depending on onset is during the first 72 hours or later. EOS occurs due to ascending infection following rupture of membranes or during passage of baby through the infected birth canal. LOS occurs mainly as nosocomial infection from the nursery or ward. The EOS infections are caused by organisms prevalent in maternal genital tract or in the delivery area. The predisposing factors include low birth weight (LBW), prolonged rupture of membranes, foul smelling liquor, multiple per vaginum examinations, maternal fever, difficult or prolonged labour and aspiration of meconium. The LOS infections are caused by the organisms thriving in the external environments of home or hospital. The infection is often transmitted through the hands of care providers. The predisposing factors include LBW, lack of breastfeeding, poor cord care, superficial infections (pyoderma, umbilical sepsis), aspiration of feeds, disruption of skin integreity with needle pricks and use of intravenous fluids. The neonatal sepsis is caused by variety of gram positive as well as gram negative bacteria and sometimes yeasts. The spectrum of organisms that causes neonatal sepsis changes over time and varies from region to region. This is due to changing pattern of antibiotic use and changes in lifestyle.

Neonates with bacterial sepsis may have either non specific signs and symptoms or focal signs of infection, including temperature instability, hypotension, poor perfusion with palor and mottled skin, metabolic acidosis, tachycardia, bradycardia, apnea, respiratory distress, grunting, cyanosis, irritability, lethargy, seizures, feeding intolerance, abdominal distension, jaundice, petechiae, purpura and bleeding. The intial manifestation may involve only limited symptomatology and only one system, such as apnea alone or tachypnea with retraction, or tachycardia or the infant may present with an acute catastrophic manifestation with multi organ dysfunction.

Early diagnosis is a key to reduce morbidity and mortality of neonatal septicaemia. The gold standard for diagnosis of septicaemia is the isolation of bacterial agents from blood culture. But definitive culture results take atleast 48-72 hours resulting in treatment delays. Hence, two-pronged approach is used for the evaluation of neonates with possible sepsis. Nonspecific sepsis screen tests like C-reactive protein (CRP), erythrocyte sedimentation rate, total white blood cell count and absolute neutrophil count are used to evaluate the likelihood of infection, and specific diagnostic tests are performed to confirm presence of a specific pathogen in body fluids.

METHODS
This prospective study was conducted in the department of pediatrics of government medical college Srinagar in collaboration with department of Microbiology of same medical college after ethical clearance from ethical committee of Government medical college Srinagar.100 neonates out of 731 neonates admitted between October 2007 and September 2008 with signs and symptoms of neonatal sepsis were included in our study by random method. Only neonates having three or more signs or symptoms of sepsis like feed refusal, lethargy, poor cry, vomiting, diarrhoea, jaundice, pyoderma, cyanosis, palor, hypothermia, fever, abdominal distension, seizures, apnea, tachypnea, grunting, poor capillary refill, umbilical discharge and sclerema were included in our study. Neonates with gross congenital anomalies including clinical suspicion of congenital heart diseases, extreme prematurity (<28weeks), severe birth asphyxia, suspected inborn errors of metabolism and respiratory distress syndrome except cases of congenital pneumonia suspected clinically in presence of risk factors. All neonates were subjected to meticulous history and examination. Routine investigations like complete blood count, absolute neutrophil count, band count, micro erythrocyte sedimentation rate, C-reactive protein, X-ray chest and abdomen in selected cases and serum biochemical investigations were done. Blood culture was done in all cases by taking 2-3ml of blood from peripheral vein under all aseptic precautions before start of antibiotics and inoculated in blood culture bottle containing 10-20ml liquid broth. Blood and broth were mixed gently and transported immediately to laboratory and incubated at 37 aerobically. The isolates were identified by Gram staining, colony characteristics and biochemical properties. Cultures were labelled negative if there was no growth after one week of incubation. Antimicrobial susceptibility of bacterial isolates was tested by Kirby Baur disc diffusion as recommended in the national committee for clinical laboratory standards (NCCLS) guidelines. Cerebrospinal fluid was taken among all neonates and was sent for culture and sensitivity besides routine examination. Data was analysed by SPSS version 15.

RESULTS
Out of 100 neonates, 51 were males and 49 were females. Blood culture was positive in 40 neonates. Significant differences have been observed regarding the blood culture positivity while assessing the differences between the early onset sepsis, place of living place of delivery,
mode of delivery, birth weight and maturity of the newborn, as is shown in Table 1.

### Table 1: Blood culture results in neonatal sepsis.

| Parameter               | Blood culture positive | Blood culture negative | P value |
|-------------------------|------------------------|------------------------|---------|
| Onset of sepsis         | Early, N=37            | 6                      | 31      | <0.001  |
|                         | Late, N=63             | 34                     | 29      |         |
| Sex                     | Male, N=51             | 26                     | 25      | <0.03   |
|                         | Female, N=49           | 14                     | 35      |         |
| Place of living         | Rural, N=61            | 28                     | 33      | <0.02   |
|                         | Urban, N=39            | 12                     | 27      |         |
| Place of delivery       | Home N=30              | 18                     | 12      | <0.03   |
|                         | Hospital, N=70         | 22                     | 48      |         |
| Mode of delivery        | Normal N=68            | 32                     | 36      | <0.001  |
|                         | LSCS N=32              | 8                      | 24      |         |
| Birth weight            | <2.5KG N=68            | 31                     | 37      | <0.02   |
|                         | >2.5KG N=32            | 9                      | 23      |         |
| Maturity                | <37weeks N=47          | 29                     | 18      | <0.001  |
|                         | >37weeks N=53          | 11                     | 42      |         |

In general, refusal of feeds is the most common symptom in neonatal sepsis, while as breathing difficulty was most common in early onset sepsis. The isolates were gram negative in 34 (85%) and gram positive in 6 (15%).

### Table 2: Clinical profile of blood culture positive sepsis.

| Symptoms          | No. of neonates | Early onset N=40 | Late onset N=34 |
|-------------------|-----------------|------------------|-----------------|
| Feed refusal      | 27 (67%)        | 2 (33.3%)        | 25 (73.5%)      |
| Lethargy          | 18 (45%)        | 2 (33.5%)        | 16 (47%)        |
| Breathing difficulty | 14 (35%)   | 5 (83.3%)        | 9 (26.4%)       |
| Hypothermia       | 12 (30%)        | 4 (66.6%)        | 8 (23.5%)       |
| Fever             | 10 (25%)        | 0 (0.0%)         | 10 (29.4%)      |
| Jaundice          | 7 (17.5%)       | 0 (0.0%)         | 7 (20.5%)       |
| Convulsions       | 7 (17.5%)       | 2 (33.3%)        | 5 (14.7%)       |

### Table 3: Organisms isolated from the studied neonates.

| Isolates                             | N=40 | Early onset N=6 | Late onset N=34 |
|--------------------------------------|------|-----------------|-----------------|
| Klebsiella pneumonia                 |      |                 |                 |
| Escherichia coli                     |      |                 |                 |
| Staphylococcus aureus                |      |                 |                 |
| Pseudomonas aeruginosa               |      |                 |                 |
| Citrobacter                          |      |                 |                 |

### Table 4: Antimicrobial susceptibility to various antimicrobials.

| Isolates                          | No. of patients | Drugs      | Sensitive | Resistant |
|-----------------------------------|-----------------|------------|-----------|-----------|
| Klebsiella pneumonia              | 15              | Amikacin   | 14 (93.3%)| 1 (6.7%)  |
|                                  |                 | Ciprofloxacin | 15 (100.00%) | 0 (0.0%)  |
|                                  |                 | Ampicillin  | 2 (13.3%) | 13 (86.7%)|
|                                  |                 | Cefotaxime  | 10 (66.6%)| 5 (33.4%) |
|                                  |                 | Ceftriaxone+sulbactum | 14 (93.3%) | 1 (6.7%)  |
| Escherichia coli                  | 13              | Amikacin   | 12 (92.3%)| 1 (7.7%)  |
|                                  |                 | Ciprofloxacin | 13 (100.00%) | 0 (0.0%)  |
|                                  |                 | Ampicillin  | 3 (23.0%) | 10 (7.7%) |
|                                  |                 | Cefotaxime  | 6 (46.2%) | 7 (53.8%) |
|                                  |                 | Ceftriaxone+sulbactum | 11 (84.6%) | 2 (15.4%) |
| Staphylococcus aureus             | 7               | Methicillin | 1 (14.3%) | 6 (85.7%) |
|                                  |                 | Vancomycin  | 7 (100.00%)| 8 (0.0%)  |
|                                  |                 | Imipenum    | 7 (100.00%)| 0 (0.0%)  |
| Pseudomonas aeruginosa            | 3               | Ciprofloxacin | 2 (66.6%)  | 1 (33.4%) |
|                                  |                 | Pipercillin+Tazobactum | 3 (100.00%)| 0 (0.0%)  |
|                                  |                 | Imipenum    | 3 (100.00%)| 0 (0.0%)  |
| Citrobacter                       | 7               | Ciprofloxacin | 2 (100.00%)| 0 (0.0%)  |
|                                  |                 | Imipenum    | 2 (100.00%)| 0 (0.0%)  |
|                                  |                 | Ceftriaxone+sulbactum | 1 (50.00%)| 1 (50.00%)|
From Table 2, onset of sepsis, sex, place of living, place of delivery, mode of delivery, birth weight, and maturity of the neonates is significantly associated with the culture positivity.

From Table 3, it is clear that feed refusal in general is most common symptom in neonatal sepsis, while as breathing difficulty was most common in early onset sepsis.

As is obvious from the results, in general, *Klebsiella pneumonia* was most organism causing neonatal sepsis and more often associated with late onset sepsis while as *Escherichia coli* was most common cause of early onset sepsis in our study.

From our study it is quite obvious that the gram-negative isolates were sensitive to aminoglycosides and cephalosporins but majority were resistant to ampicillin as is depicted in Table 4. It is pertinent to mention that methicillin resistance against staph aureus is quite high in our setting.

The mortality rate in neonatal sepsis turned 35% in our study. From our results neonates with pseudomonas infection were having highest mortality followed by *Citrobacter* and staph aureus as is shown in Table 5.

## DISCUSSION

The uncertainty surrounding the clinical approach to treatment of neonatal septicemia can be minimized by periodic epidemiologic surveys of aetiological agents and their antibiotic sensitivity patterns leading to recognition of the most frequently encountered pathogen in a particular geographic area. Our study was similar one and it supported the findings of previous studies. The blood culture positivity rate of 40% in our study was similar to studies done by Ahmed ANU et al and Shukla et al.11,12 The high positive culture rate in recent studies than older studies like Mathur M et al, is probably due to improved techniques of bacterial isolation and availability of rapid diagnostic kits.13 As reported by Ahmed ANU et al, our study shows that incidence of neonatal sepsis is more common in male babies (50.98% vs 28.72%) which could be due to some social factors with bias in gender towards patient treatment.11 The late onset sepsis was more common than early onset (85% vs 15%) similar to early studies like Ahmed ANU et al and Taller SS et al.11,15 The higher incidence of late onset sepsis may be because of use of 72hrs as cutoff for defining early onset sepsis and its higher mortality. Neonatal sepsis was more common in neonates born in rural than in urban (70% vs 30%) similar to studies like Taller SS et al, Rasul CH et al and Iyer CR et al.3,14,15 This could be because of differences in delivery places and lack of trained knowledgeable health care providers in rural areas which may also be reason for higher incidence of sepsis in normal vs caesarean deliveries (80% vs 20%). Our study revealed that neonatal sepsis is more common in low birth babies than normal weight babies (77.5% vs 22.5%) in accordance to studies of Iyer CR et al and Rajana R et al.13,15 The could be because of immunological immaturity and overall high risk behavior of low birth neonates. Refusal of feeds and lethargy were most common symptoms of neonatal sepsis (67.5% vs 45%) consistent with Jaswal RS et al.16 The gram negative organisms were isolated in 85% of cases consistent with studies done by Mathur M et al, Rasul CH et al and Jaswal RS et al.13,14,16 The most common organisms isolated in our study were klebsiella pneumonia (40%), *Escherichia coli* (32.2%) and *Staphylococcus aureus* (15%) in that order consistent with Taller SS et al.7 The probable reason for it being that most of gram negative organisms are normal commensals and neonates are less protected against them because of low IgM antibodies. The rarity of group B streptococcus in our study could be due to its low prevalence in our settings. The gram negative isolates were sensitive to aminoglycosides and cephalosporins but majority were resistant to ampicillin similar to studies done by Taller SS et al and Rasul CH et al.5,14 99% of staphylococcus isolates were sensitive to vancomycin and imipenem but 85% were resistant to methicillin consistent with Ahmed

| Parameter       | No. of patients | Patients died | Mortality rate |
|-----------------|-----------------|---------------|----------------|
| Onset of sepsis |                 |               |                |
| Early           | 6               | 3             | 50%            |
| Late            | 34              | 11            | 32%            |
| Birth weight    |                 |               |                |
| <2.5kg          | 31              | 13            | 41.9%          |
| >2.5kg          | 9               | 1             | 11.1%          |
| Maturity        |                 |               |                |
| <37             | 29              | 13            | 44.8%          |
| >37             | 11              | 1             | 9%             |
| Isolates        |                 |               |                |
| *Pseudomonas aeruginosa* | 3        | 2             | 66%            |
| *Citrobacter*   | 2               | 1             | 50%            |
| *Klebsiella pneumonia* | 16    | 7             | 43.6%          |
| *Staphylococcus aureus* | 6       | 2             | 33%            |
| *Escherichia coli* | 13         | 2             | 15.3%          |
ANU et al and Rasul C H et al.11,14 Mortality in our study 35% consistent with Ahmed ANU et al and Shukla et al (41%).11,12 Mortality was higher early onset sepsis than late onset sepsis (50% vs 32%) in accordance with Ahmed ANU et al and in low birth babies than normal weight babies (41.9% vs 11.1%) in accordance with Ahmed ANU et al and Taller SS et al.11,5 In our study mortality due to pseudomonas was highest (66%) and least with Escherichia coli (15%) in accordance with Ahmed ANU et al.11

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