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**Original Research Article**

# Clinical profile, cardiac involvement and outcome of children admitted with sepsis in pediatric intensive care unit at GB Pant children hospital Srinagar

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## ABSTRACT

**Background:** Sepsis is a systemic illness caused by an infectious agent invading the body, which induces the release of inflammatory mediators, resulting in systemic inflammatory response syndrome (SIRS). The aim of our study was to recognize clinical profile, cardiac involvement, laboratory work up, etiology, treatment, and immediate outcome of patients admitted with sepsis.
**Methods:** This prospective observational study was conducted in pediatric intensive care unit over period of two years. After informed consent from parents, all those patients meeting inclusion criteria were subjected to complete history, general and systemic physical examination. Routine baseline investigations included CBC, LFT, KFT, ABG, chest X-ray, serum calcium and phosphorous were done in all patients. The other investigations like echocardiography, COVID-19 RAT and RTPCR, CSF, blood and urine culture, USG, CT, MRI and various inflammatory markers like serum ferritin, CRP and ESR whenever required were done.
**Results:** In this study 35 patients aged 1 year to 18 years with a diagnosis of sepsis were included. Out of them 20 were males and 15 were females with a male female ratio of 1.3:1 and mean age of 6.2 years. The most common etiology for sepsis was severe pneumonia seen in 17 (48.5%) cases while 8 (22.9%) had osteomyelitis, 3 (8.6%) had urinary tract infection, 2 (5.7%) had meningoencephalitis, 2 (5.7%) had severe diabetic ketoacidosis with culture proven sepsis, 2 (5.7%) had gastrointestinal infection and 1 (2.86%) had iliopsoas abscess with liver abscess. On echocardiography 9 (25.7%) patients had left ventricular (LV) dysfunction with left ventricular ejection fraction (LVEF) less than 55% and 3 (8.6%) patients had pericardial effusion. Out of them 20 (57%) patients were discharged after 8.9 days mean duration of hospital stay and 15 (43%) patients got expired after 3.1 days mean duration of hospital stay.
**Conclusions:** Severe sepsis with septic shock is the leading cause of mortality if not picked early and treated aggressively.

**Keywords:** Echocardiography, Multi-organ dysfunction syndrome, Sepsis, Septic shock

## INTRODUCTION

Sepsis is a systemic illness caused by an infectious agent invading the body, which induces the release of inflammatory mediators, resulting in systemic inflammatory response syndrome (SIRS). Mortality for children with sepsis ranges from 4% to as high as 50%, depending on illness severity, risk factors, and geographic location. Infectious diseases account for approximately 60% of deaths in children with sepsis younger than 5 years old.[1] The majority of children who die of sepsis suffer from refractory shock and/or multiple

organ dysfunction syndrome, with many deaths occurring within the initial 48-72 hours of treatment. Early identification and appropriate resuscitation and management are therefore critical to optimizing outcomes for children with sepsis.[2]

Sepsis can be caused by bacterial, viral, fungal, parasitic, and rickettsial infections. Bacteria and viruses are the most frequently identified pathogens. The most frequent sites of infection in children with severe sepsis, are the lungs (50-60%), abdomen (20-25%), urinary tract (7-10%), the central nervous system (<5%) and blood stream (<5%). Bacteremia occurs in 40-60% of patients with septic shock.[3]

The aim of our study was to recognize clinical profile, cardiac involvement, laboratory work up, etiology, treatment, response to treatment and immediate outcome of patients admitted with sepsis in our pediatric intensive care unit.

## METHODS

The study was prospective and observational conducted over a period of two years (December 2020-November 2022) in the pediatric intensive care unit of the GB Pant children hospital, postgraduate department of pediatrics GMC Srinagar, which is a tertiary care hospital for the children of Kashmir valley. Our study was approved by the ethical committee of Government Medical College Srinagar via communication n (Minutes-BOPGS) Acad/KU/22 02-02-2022 held on 29 and 30th September, 2021 under serial number 8. After informed consent from parents, all those patients meeting inclusion criteria were subjected to complete history, general and systemic physical examination. Routine baseline investigations included CBC, LFT, KFT, ABG, chest X-ray, serum calcium and phosphorous were done in all patients. The other investigations like echocardiography, troponin-T, COVID-19 RAT and RTPCR, CSF, blood and urine culture, USG, CT, MRI and various inflammatory markers like serum ferritin, pro-calcitonin CRP and ESR whenever required were done.

### *Inclusion criteria*

Patients with age >1 year and <18 years admitted in pediatric intensive care unit with a diagnosis of sepsis by clinical and/or laboratory parameters.

### *Exclusion criteria*

Patients with PICU stay of less than 6 hours, congenital or acquired heart disease, neurodevelopmental delay, neuropathy/myopathy, genetic syndromes, congenital malformations, postoperative patients, cardiopulmonary arrest at the time of admission, cardiac surgery within last 3 months, age <1 year and >18 years, and burns/major trauma were excluded from the study.

### *Statistical analysis*

Data was entered in a Microsoft Excel spreadsheet and analyzed using SPSS version 22 software. Categorical variables were summarized as frequency and percentage. Continuous variables were summarized as mean and SD.

### *Determination of sample size*

Using GPOWER software (version 3.0.10), was estimated that the least number of patients required with 80% power, 5% significance level and an effect size of 0.39 was 35. Therefore, we included a total of 35 patients in our study.

## RESULTS

In this study 35 patients aged 1 year to 18 years with a diagnosis of sepsis were included. Out of them 20 were males and 15 were females with a male female ratio of 1.3:1 a mean age of 6.2 years as depicted in Table 1. In this study 20 (57%) patients were discharged after 8.9 days mean duration of hospital stay and 15 (43%) patients got expired after 3.1 days mean duration of hospital stay.

**Table 1: Gender distribution, mean age and mean duration of hospital stay in study population.**

| Gender | Frequency | Percentage | Mean duration of hospital stay | Mean age |
|---|---|---|---|---|
| **Male** | 20 | 57 | | |
| **Female** | 15 | 43 | 8.9 days | 6.2 years |
| **Total** | 35 | 100 | | |

The most common etiology for sepsis was severe pneumonia seen in 17 (48.5%) cases while 8 (22.9%) had osteomyelitis, 3 (8.6%) had urinary tract infection, 2 (5.7%) had meningoencephalitis, 2 (5.7%) had severe diabetic ketoacidosis with culture proven sepsis, 2 (5.7%) had gastrointestinal infection and 1 (2.86%) had iliopsoas abscess (blood culture positive for MRSA) with liver abscess. The patients presented with different symptoms. Fever was the most common presenting symptom. The different symptoms along with their frequencies are shown in Table 2.

Most common sign in sepsis patients was fever in 33 (94.3%) patients, Followed by hypotension in 33 (94.3%)

patients, tachycardia in 32 (91.4%) patient and respiratory distress in 30 (85.7%) patients. Other common signs are listed in Table 3.

**Table 2: Symptoms in sepsis patients.**

| Symptoms | No. of patients (n=35) | Percentage |
|---|---|---|
| **Fever** | 33 | 98.7 |
| **Vomiting** | 14 | 40 |
| **Cough** | 13 | 37 |
| **Fast breathing** | 13 | 37 |
| **Pain abdomen** | 11 | 31.4 |
| **Loose stools** | 8 | 22.8 |
| **Swelling over limb** | 6 | 17.1 |
| **Lethargy** | 4 | 11.4 |
| **Rash** | 4 | 11.4 |
| **Re eyes** | 4 | 11.4 |
| **Headache** | 3 | 8.6 |
| **Abnormal body movements** | 2 | 5.7 |
| **Blood with urine** | 1 | 2.85 |

In this study 32 (91.4%) patients had leukocytosis, 22 (63%) patients had neutrophilia, 1 (2.8%) patient had normal leukocyte count and 2 (5.7%) patients had leucopenia. Thrombocytopenia was seen in 13 (37%) patients and 22 (63%) patients had normal platelet count. Hemoglobin was low in 22 (63%) patients and normal in 13 (37%) patients. In biochemistry KFT was deranged in 8 (23%) patients, liver enzymes were elevated in 6 (17%) patients with 4 (11.4%) patients had raised bilirubin, 1 (2.8%) patient had low albumin levels and serum calcium was low in 3 (8.6%) patients. Among inflammatory markers, CRP was positive in all 35 (100%) patients, ESR was raised in 33 (94.3%) patients, LDH was raised in 20 (57%) patients and Ferritin was raised in 24 (68.6%). Fibrinogen was done in 4 patients (n=4) and was raised in 3 (75%) patients and d-dimer was done in 4 patients and was positive in all of them. On arterial blood gas analysis metabolic acidosis was the most common abnormality seen in 30 (85.7%) patients followed by respiratory acidosis in 4 (11.4%), hyperlactatemia in 28 patients (80%), hypernatremia in 4 (11.4%) and hyponatremia in 2 (5.7%) patients.

**Table 3: Different signs in sepsis patients.**

| Signs | No. of patients (n=35) | Percentage |
|---|---|---|
| **Fever** | 33 | 94.3 |
| **Hypotension** | 33 | 94.3 |
| **Tachycardia** | 32 | 91.4 |
| **Tachypnea** | 30 | 85.7 |
| **Respiratory distress** | 16 | 45.7 |
| **Lethargy/drowsiness** | 8 | 22.8 |
| **Pallor** | 6 | 17.1 |
| **Signs of dehydration** | 6 | 17.1 |
| **Agitated /irritable behavior** | 6 | 17.1 |
| **Swelling over a limb** | 6 | 17.1 |
| **Encephalopathy** | 5 | 14.3 |
| **Abdominal tenderness** | 5 | 14.3 |
| **Rash** | 5 | 14.3 |
| **Convulsions** | 2 | 5.7 |
| **Conjunctivitis** | 2 | 5.7 |
| **Lymphadenopathy** | 1 | 2.8 |
| **Strawberry tongue** | 1 | 2.8 |

**Table 4: Organisms isolated in different body fluids/specimens.**

| Organism | Blood n (%) | Urine n (%) | Pleural fluid n (%) | ET tip n (%) | CVL catheter tip n (%) | Abscess/ bone drain fluid n (%) | Total |
|---|---|---|---|---|---|---|---|
| **MRSA** | 2 | | | | 1 | 1 | 4 |
| **MSSA** | 3 | | | | | 1 | 4 |
| ***Klebsiella*** | 1 | 1 | 1 | | | | 3 |
| ***Escherichia coli*** | | 1 | | | | | 1 |
| **Acinetobacter** | | | | 1 | | | 1 |
| **Pseudomonas** | | | | 1 | | | 1 |

In the study on echocardiography 9 (25.7%) patients had left ventricular (LV) dysfunction with left ventricular ejection fraction (LVEF) less than 55% and 3 (8.6%) patients had pericardial effusion. Among patients with LV dysfunction, 3 had mild LV dysfunction (EF=41-55%), 4 had moderate LV dysfunction (EF=31-40%) and 2 patients had severe LV dysfunction (EF≤30%).

In this study blood culture was positive in 6 (17.1%) patients. Staphylococcus was the most common organism isolated. The details of the organisms isolated in blood, urine, pleural fluid, endotracheal tube (ET) tip, central venous line (CVL) catheter and abscess/bone drain fluid is shown in Table 4.

## DISCUSSION

In this study 35 patients were admitted as cases of severe sepsis or septic shock. 20 patients were females and 15 (43%) were males. Similar results were reported by Kurade et al, with males being 46.5% of all cases.[4] In our study mean age of cases was 6.2 years which resembled study by Tonial et al showing mean age of 6 years in severe sepsis cases.[5] Similarly a European study by Boeddha et al reported mean age of 7 years and another study from Nepal by Ghimire et al showed mean age of 7.4 years.[6,7] Fever was most common symptom at the time of PICU admission in 94.3% sepsis patients which is comparatively more in comparison to Bhatta et al and Kurade et al showing fever in 81% and 62.8% patients respectively.[8,4] Respiratory system manifestations were seen in 85% sepsis patients in our study mainly in the form of cough and respiratory distress. Similar results were seen in studies by Xiao et al and Bhatta et al with respiratory system involvement in 76.7% and 86% patients respectively.[9,8] Gastrointestinal symptoms were seen in 54.3% sepsis patients in our study. Mainly in the form of vomiting, loose stools and pain abdomen. However, pain abdomen and tenderness were present on examination in 14% patients only. Consequently, one patient (2.86%) was diagnosed as case of liver abscess and 3 (8.6%) patients as cases of UTI with klebsiella grown in one urine culture. Similar results were reported by Kurade et al showing 9% sepsis patients with UTI and abdominal infections.[4] On contrary, Bhatta et al reported gastrointestinal causes of sepsis in 18.6% patients.[8]

In our study 94.3% sepsis patients were in shock at the time of admission to PICU. Similarly, Bhatta et al reported shock in 79% sepsis patients at the time of admission to PICU.[8] Our results are in contrary to other studies where the prevalence of shock at admission varies from 50.4% to 74.4%.[4,6,10] One possible reason could be non-availability of beds in hospitals during COVID-19 2nd wave leading to late presentation to the hospital or the more number of osteomyelitis cases in our study with advanced disseminated sepsis in most cases. In our study neurological manifestations were observed to be present in 60% sepsis patients which resembled the findings of a study by Bhatta et al showing neurological manifestations in 67% of severe sepsis patients.[8] However, it was in contrary to findings of Tonial et al and Kaur et al showing neurological involvement in 15% and 12% patients respectively.[5,11] In our study 2 (5.7%) patients were cases of meningoencephalitis which resembled the results obtained by Humoodi et al showing meningoencephalitis in 5.3% patients among severe sepsis cases in PICU.[10] Whereas it was in contrary to Boeddha et al and Ismail et al reporting meningoencephalitis in 23% and 25% sepsis patients admitted in ICU respectively.[6,12] In our study 8 (23%) patients were cases of sepsis with no focus including 2 patients of severe DKA with sepsis. Boeddha et al reported sepsis without a focus in 35% of sepsis patients admitted in intensive care.[6] In our study 20% sepsis patients were blood culture documented blood stream infections. *Staphylococcus aureus* was grown in 5 patients and *Klebsiella* species in 1 patient. Similar results were reported by Kurade et al and Bhatta et al with *Staphylococcus aureus* to be most common cause of blood stream infections in pediatric severe sepsis.[6,9] Humoodi et al also reported blood stream infections in 26.5% patients with severe sepsis patients admitted in PICU.[10] In our study 43% patients were admitted as cases of pneumonia and/empyema which was similar to the results observed by Ghimire et al showing pneumonia in 46.8% of severe sepsis patients in intensive care.[7] Similar results were also reported by Xiao et al and Ismail et al with pneumonia in 37.6% and 47.5% patients respectively.[9,12] In our study 20% sepsis patients presented with symptoms of pain and swelling over limbs, and 6 cases were diagnosed as osteomyelitis and one case as iliopsoas muscle abscess. Similar results were reported by Kurade et al with 30% sepsis patients in intensive care admitted as cases of bone, joint, skin and soft tissue infections.[4] In our study 91.4% patients had leukocytosis, 5.7% patients had leucopenia, 37% had thrombocytopenia, 63% had anemia which was in conformity with the Kurade et al who reported leucocytosis in 60.46%, leucopenia in 13.9%, thrombocytopenia in 56% and anaemia in 62.7% severe sepsis patients.[4] AKI was present in 23% sepsis patients in our study and similar results were seen by Bhatta et al with AKI in 30% patients admitted to PICU with severe sepsis.[8] In another Indian study AKI was seen in 14% patients as reported by Baranwal et al.[16] Liver dysfunction was seen in 17.1% sepsis patients in our study. In contrast, Kurade et al reported liver dysfunction in 86% sepsis patients.[4] This difference is significant and can be correlated with 90% MODS and 60% mortality in study by Kurade et al as compared to 43% MODS and mortality in our study.[4] In our study 3 (50%) patients, among 6 cases of *Staphylococcus aureus* sepsis patients, developed pericardial effusion which resembled a study by Kabra et al showing pericardial effusion in 50% patients with disseminated staphylococcus aureus sepsis.[14] Left ventricular systolic dysfunction (LVEF<55%) was seen in 25.7% sepsis patients in our cohort. Same results were reported by Baranwal et al with LV dysfunction in 26% patients.[13] Similar reports were

observed by Tonial et al Jain et al and Raj et al showing LV dysfunction in 30%, 21.3% and 37% patients respectively.[5,15,16] In contrast, Ismail et al, Williams et al and Lautz et al reported LV dysfunction in 47.5%, 44% and 18% sepsis patients respectively.[12,17,18] Troponin-t was positive in 28.6% sepsis patients in our study similar results were also reported by Raja et al with troponin-t positive in 27.75% sepsis patients.19 In our study 94.3 sepsis patients were managed as septic shock and received inotropic and vasoactive drugs, i.v. fluids and antibiotics. MODS developed in 43% sepsis patients. 11.4% patients received IVIG and 17.1% patients received steroids, 37.1% patients required mechanical ventilation and 28.6% patients received blood transfusions. Mortality was 43% (15 patients died in PICU) in sepsis patients in our study. Similar mortality rates were observed by Kaur et al with a mortality rate of 42% in sepsis patients in intensive care.[12] Similarly, Bhatta et al reported mortality of 51.2% in patients with severe sepsis and septic shock.[8] A study by Carmona et al reported mortality of 30% in severe sepsis patients.[20] Kurade et al conducted a study in India and reported a mortality of 60.46% in paediatric sepsis in intensive care.[4] Mean duration of hospital stay of sepsis patients in our study was 8.9 days similar to some other studies.[11-13]

This study has certain limitations. Smaller sample size is one of the limitations of the study and also some patients received treatment prior to arrival at our centre, this could have masked many clinical and laboratory findings. Similar study, with a larger sample size could be done in the future to get a clearer picture.

## CONCLUSION

This study showed younger children are vulnerable to sepsis. Pneumonia is the most common etiology. Most of the patients who developed sepsis presented in septic shock. The presence of severe sepsis, ARDS, DIC, hyperlactatemia, metabolic acidosis was associated with increased hospital stay and mortality.

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