

## Original Research Article

# Clinical profile and outcome of organ dysfunction in sepsis

**Laxmikanta Dash, Lagendra Kumar Singh\*, Malati Murmu, Susruth Krishnadas P.,  
Amita Kerketta, Mrutyunjay B. Hiregoudar**

Department of Medicine, VSSIMSAR, Burla, Sambalpur, Odisha, India

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**\*Correspondence:**

Dr. Lagendra Kumar Singh,

E-mail: [drlagendra88@gmail.com](mailto:drlagendra88@gmail.com)

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### ABSTRACT

**Background:** Sepsis is defined as life threatening organ dysfunction due to a dysregulated host response to infection. It is the tenth leading cause of death among older adults in United States. Mortality rate of the sepsis ranges from 30-40%. In severe cases sepsis can drastically reduce blood flow to the major organs, leading eventually to septic shock, widespread organ failure and death. So, the present study was done to evaluate the clinical profile, symptoms, source of infection, co-morbid conditions and outcome with respect to the organ dysfunction in sepsis cases.

**Methods:** This prospective observational study was undertaken among 100 cases of sepsis diagnosed by the "International Sepsis Definitions Conference" criteria admitted during October 2015 to September 2017. All patients were evaluated clinically and subjected for laboratory investigations.

**Results:** In present study, a total of 100 cases were enrolled. Mean age of cases were 38.15 years. Male and female ratio was 1.63:1. Most common symptom was fever (100%). Pneumonia was the most common (36%) source of infection. Mortality was highest in pneumonia (55.55%). 77 % of cases had organ dysfunction. Cardiovascular system was the most common system involved. Maximum mortality was within the age group of 56-65 years. Diabetes was the most common co-morbid condition. Mean APACHE II score was high among the death cases.

**Conclusions:** Sepsis was more common in younger group of patients but mortality was more in elderly age group. Overall mortality was 38%.

**Keywords:** APACHE II, MODS, Outcome, Sepsis, Vasopressors

### INTRODUCTION

Sepsis is defined as life threatening organ dysfunction due to a dysregulated host response to infection.<sup>1</sup> It is one of the most important causes of death in hospitalized patients. It remains the most important cause of multi-organ dysfunction syndrome (MODS) all over the world.<sup>2,3</sup> Sepsis is now the tenth leading cause of death among older adults in the United States. Over the last decade, sepsis has become more common and deadly to the society.<sup>4-6</sup> Mortality rate of sepsis ranges from 30-40%.<sup>7-9</sup> Data from the developing countries is scarce.<sup>10,11</sup> In a multicentric study in ICU setting from India, the

incidence and in-hospital mortality rate of severe sepsis were 16.45% and 65% respectively.<sup>12</sup>

Pathophysiology of sepsis is complex and multifactorial. Infection triggers pro-inflammatory and anti-inflammatory response that contribute to the control of infection as well as the tissue damage that leads to organ failure. In its most severe form, sepsis can drastically reduce blood flow to the major organs, leading eventually to septic shock, widespread organ failure and death.<sup>13</sup>

There is a paucity of studies regarding the clinical profile and outcome of organ dysfunction in sepsis patients in this part of the country. The present study was an effort to

evaluate the clinical profile of the sepsis patients, their symptoms, source of infection, co-morbid conditions and outcome with respect to the organ dysfunction in the cases.

The primary objective of this study was to evaluate the clinical profile of organ dysfunction in sepsis and secondary one is to study the outcome in different organ dysfunction cases.

## METHODS

The present study was a hospital based prospective observational study carried out in the department of Medicine, VSS Institute of Medical Sciences and Research, Sambalpur in the state of Odisha from October 2015 to September 2017. Ethical approval was obtained from the Institutional Ethics Committee (IEC) and informed consent was taken from either the patients or their relatives.

In this study 100 no of patients admitted to Medicine wards or Central ICU and diagnosed to have sepsis according to the “International Sepsis Definitions Conference” criteria coined by Levy MM et al, satisfying the inclusion and exclusion criteria were enrolled.<sup>14</sup>

### Inclusion criteria

- Any patient age >15 years with clinical and laboratory evidences of sepsis as per the International Sepsis Definitions Conference criteria.<sup>14</sup>
- Both sexes

Septic shock was diagnosed as sepsis with hypotension (arterial BP<90mmHg systolic or 40 mm less than patient's normal BP) for at least 1 hour despite adequate fluid resuscitation or need for vasopressors to maintain systolic blood pressure  $\geq$ 90mmHg or MAP  $\geq$ 70mm Hg.

Patients were considered to have organ dysfunction when:

- Cardiovascular: Arterial hypotension (SBP <90mmHg, MAP <70mmHg or an SBP decrease by >40mmHg)
- Respiratory: Arterial hypoxemia ( $\text{PaO}_2/\text{FiO}_2 < 300$ )
- Renal: Acute oliguria (urine output <0.5ml/kg/hr for at least 2 hours despite adequate fluid resuscitation) or increase in creatinine >0.5mg/dl
- Hematological: Coagulation abnormalities (INR>1.5) or thrombocytopenia (platelet count <100,000/ $\mu\text{l}$ )
- Hepatic: Plasma total bilirubin>4 mg/dl

### Exclusion criteria

Patients with,

- Postoperative cases of sepsis
- Posttraumatic cases of sepsis

- Acute pancreatitis
- Sepsis due to burn injury
- Pericardial tamponade

Detailed history and thorough clinical examination was performed on each patient. Different laboratory investigations like complete blood count (CBC), blood urea, serum creatinine, serum sodium and potassium, blood glucose, liver function tests, HIV, HCV, HBV, ESR, CRP, PT/INR, MP slide/QBC, arterial blood gas (ABG) analysis, blood culture, plasma lactate, urinalysis with culture, sputum gram stain and culture, chest-x-ray, ultrasonography of abdomen were done. Demographic data, clinical features, relevant laboratory parameters and clinical course of the patients were recorded in a structured proforma. APACHE II score of each patient was calculated within 24 hours of admission using the scoring system developed by Knaus WA et al.<sup>15</sup> Data collected were tabulated, analyzed, using Microsoft Office Windows 2008 and compared with the previous studies.

## RESULTS

In present study, maximum no (29%) of patients belong to 16-25 years of age group followed by 24% in 26-35 years. No patients were admitted above 85 years of age. Majority of male patients (23%) were in 16-25 years age group and majority of female patients (13%) in the age group of 26-35 years (Table 1).

**Table 1: Age and Sex distribution of cases.**

Age group	No of cases		Total
	Male	Female	
16-25	23	06	29
26-35	10	14	24
36-45	12	05	17
46-55	05	08	13
56-65	06	05	11
66-75	02	00	02
76-85	04	00	04
>85	00	00	00
Total	62	38	100

Fever was the most common presenting symptom present in all cases followed by altered sensorium, cough and dyspnoea in 52, 44 and 43 cases respectively (Table 2).

Fever was the most common clinical presentation in all diseases. All pneumonia cases had cough and 35 had difficulty in breathing. Chest pain was present in 19 cases of pneumonia. Altered sensorium was present in 18 cases of pneumonia, 16 cases of malaria, 2 cases of UTI, 11 cases of meningo-encephalitis and 5 cases of unspecified infection. Hypotension was present in 23 cases of pneumonia, 9 cases of malaria, 1 case of UTI and 4 cases of meningo-encephalitis. Vasopressor was required to maintain blood pressure in 10 cases of pneumonia, 9

cases of malaria, 1 case of UTI and 3 cases of meningo-encephalitis (Table 3).

In this study, most common infection was pneumonia constituting 36 (36%) cases followed by UTI, malaria and meningo-encephalitis. Mortality was highest in pneumonia with 20 (55.55%) followed by malaria with 10 (52.63%) and lowest in UTI with 2 (10.52%) (Table 4).

In this study, organ dysfunction in males was highest (16%) in 16-25 years of age group followed by 36-45 (10%) years. In females organ dysfunction was highest in 26-35 years (9%) followed by 46-55 years (8%) of age group (Table 5).

**Table 2: Distribution of symptoms among cases of sepsis.**

Symptoms	No of cases	Percentage (%)
Fever	100	100
Cough	44	44
Dyspnoea	43	43
Chest pain	22	22
Vomiting	36	36
Loose stool	08	08
Abdominal pain	28	28
Decreased urination	29	29
Altered sensorium	52	52
Convulsion	07	07
Jaundice	23	23

**Table 3: Correlation of clinical features and diseases.**

Clinical features	Pneumonia	Severe malaria	UTI	Meningo-encephalitis	Others/ unspecified
Fever	36	19	19	11	15
Cough	36	06	00	00	02
Dyspnoea	35	06	00	00	02
Chest pain	19	02	00	00	01
Vomiting	06	10	12	05	03
Abdominal pain	07	03	10	03	05
Oliguria	03	12	06	02	06
Altered sensorium	18	16	02	11	05
Jaundice	02	16	00	00	05
Convulsion	01	03	00	03	00
Tachycardia	36	19	19	11	15
Tachypnoea	36	08	02	00	04
Hypotension	23	09	01	04	06
Vasopressor requirement	10	09	01	03	04

**Table 4: Various diseases and outcome in sepsis**

Diseases	No of patients	No of death	Percentage of mortality
Pneumonia	36	20	55.55%
Severe malaria	19	10	52.63%
Urinary tract infection	19	02	10.52%
Meningoencephalitis	11	03	27.27%
Others/Unspecified	15	03	20%
Total	100	38	38%

Cardiovascular system was the most common organ dysfunction, found in 50 (64.93%) cases with 27 cases of pneumonia, 12 cases of malaria, 5 cases of Meningoencephalitis, 4 cases of unspecified infection and 2 cases of UTI. Next common organ dysfunction was renal seen in 48 (62.33%) cases, out of which 10 cases were pneumonia, 16 were malaria, 11 were UTI, 7 were

unspecified infection and 4 cases were of Meningoencephalitis.

**Table 5: Age and sex wise distribution of organ dysfunction in sepsis.**

Age group	No of cases with organ dysfunction		Total	Percentage (%)
	Males	Females		
16-25	16	05	21	21
26-35	09	09	18	18
36-45	10	05	15	15
46-55	03	08	11	11
56-65	04	03	07	07
66-75	02	00	02	02
75-85	03	00	03	03
>85	00	00	00	00
Total	47	30	77	77

Respiratory system was involved in 31 (4.25%) cases with pneumonia of 25 cases, malaria of 4 and UTI and unspecified infection of 1 case each. G.I system and

hematological systems were affected in 18 (23.37%) cases each (Table 6).

**Table 6: Organ dysfunction in various diseases.**

Systems involved	Pneumonia	Malaria	UTI	Meningoencephalitis	Others/unspecified	Total cases (%)
CVS	27	12	02	05	04	50 (64.93%)
Renal	10	16	11	04	07	48 (62.33%)
Respiratory	25	04	01	00	01	31 (40.25%)
G.I. system	02	16	00	00	00	18 (23.37%)
Hematological	01	13	00	02	02	18 (23.37%)

According to assessment of organ dysfunction in course of hospital stay, 24 had single organ dysfunction, 22 had two organ dysfunction and 31 cases had multi-organ dysfunction.

Mortality was lowest in single organ dysfunction cases with 1 (4.16%) and highest with 25 (80.64%) when more than two organ (multi) dysfunction was present. There was a statistically significant increase in mortality with progressive rise in no of organ dysfunction (p value<0.0001) (Table 7).

Cardiovascular and renal combination involvement was maximum (32%) followed by respiratory and renal and respiratory and hematological system which is 5% in each combination (Table 8).

Maximum mortality in this study was within age group of 56-65 years (54.54%) and minimum was within age group of 46-55 years (23.07%) (Table 9).

**Table 7: Outcome of organ dysfunction cases during hospital stay.**

Organ dysfunction	Total patients	Patients survived	Death	Percentage of mortality
Single organ dysfunction	24	23	01	4.16%
Two organ dysfunction	22	10	12	54.54%
More than two organ dysfunction	31	06	25	80.64%
Total	77	39	38	49.35%

In this study, diabetes mellitus was the commonest co-morbidity, present in 13 patients. Out of 13 patients, 8 (61.53%) had organ dysfunction with mortality of 5 (27.7%) but mortality was 100% in co-morbid conditions like, CML, CKD and Rheumatoid arthritis (Table 10).

**Table 8: Combination of multi-organ dysfunction in sepsis.**

Organ dysfunction	Cardiovascular	Respiratory	Renal	G.I. System	Haematological
Cardiovascular	-	29	32	15	16
Respiratory	29	-	16	05	05
Renal	32	16	-	17	17
G.I. System	15	05	17	-	13
Haematological	16	05	17	13	-

**Table 9: Outcome according to age group.**

Age group	Total no of patients	Mortality		Total mortality (%)
		Male	Female	
16-25 years	29	06	02	8(27.58)
26-35 years	24	04	06	10(41.66)
36-45 years	17	04	04	8(47.05)
46-55 years	13	02	01	3(23.07)
56-65 years	11	03	03	6(54.54)
66-75 years	02	01	00	1(50)
76-85 years	04	02	00	2(50)
Total	100	22	16	38(38%)

**Table 10: Organ dysfunction and outcome in patients with co-morbidities with sepsis.**

Co-morbidities	No of patients	Patients with organ dysfunction	Percentage of patients with Organ dysfunction	Death	Mortality percentage (%)
Diabetes mellitus	13	08	61.53	05	27.7
CML	02	02	100	02	100
RHD	02	02	100	00	00
Sickle Cell Disease	05	04	80	03	60
CKD	01	01	100	01	100
Hypertension	01	01	100	00	00
Rheumatoid arthritis	01	01	100	01	100
HIV	01	01	100	00	00
Total	26	20	76.92	12	46.15

**Table 11: Apache score and outcome in cases of sepsis.**

	All patients	Survived	Death
Mean Apache score	14.87	10.16	22.55
Standard deviation	±7.13	±3.83	±4.28

Mean APACHE-II score of the patients having organ dysfunction was 14.87 with standard deviation of  $\pm 7.13$  (Table 11).

Mechanical ventilation was given to 31 cases, out of which 7 (22.6%) patients survived and 24 (77.4%) died. 28 patients were put on renal replacement therapy (haemodialysis), 19 (67.9%) patients survived and 9 (32.1%) patients expired. Vasopressors support was required in 27 patients, out of which 6 (22.2%) cases survived and 21 (77.8%) died (Table 12).

**Table 12: Interventional modalities and outcome in sepsis.**

Modalities	Total patients	Survivor (%)	Death	Percentage of death (%)
Vasopressors	27	06 (22.2%)	21	77.8
Mechanical ventilation	31	07 (22.6%)	24	77.4
Renal replacement therapy (Hemodialysis)	28	19 (67.9%)	09	32.1

## DISCUSSION

The present study included 100 patients diagnosed with sepsis according to the inclusion criteria. Lowest age was 16 and highest was 85 years. Mean age was 38.15 years with a standard deviation of  $\pm 16.97$ . Maximum no 29 (29%) of patients were from 16-25 years of age group. In contrast to our study, Bhattacharyya PK et al and Gaieski DF et al had found majority of patients in age group of >65 years.<sup>16,17</sup> Male population in the study was 62% and female was 38% with male to female ratio of 1.63:1. Paary TTS et al, and Todi et al, had found 64.2% and 57.71% of male patients respectively in their studies which is similar to our study.<sup>18,19</sup>

Fever was the most common presenting symptom in all cases followed by altered sensorium, cough and dyspnoea in 52, 44 and 43 cases respectively. Bhattacharyya et al also observed fever as the predominant symptoms in their study.<sup>16</sup>

In this study, pneumonia was the most common source of infection comprising of 36 (36%) cases, followed by

malaria, UTI, unspecified infection and meningococcal encephalitis. TTS Paary et al, had similar observation with source of infection in the respiratory tract (37.2%), whereas Simon F et al, Engel C et al, Karlsson S et al, and Desai SR et al, showed different source of infections.<sup>8,18,20-22</sup> Mortality was highest in pneumonia with 20 (55.55%), followed by malaria with 10 (52.63%) and lowest in UTI with 2 (10.52%). Fedili U et al, also observed respiratory tract infection as the commonest (40%) cause of mortality like our study, whereas Leligdowicz A et al, reported ischemic bowel as the highest (75%) cause of mortality among severe sepsis cases.<sup>23,24</sup>

Present study had 77 cases (77%) of organ dysfunction developed during the course of hospital stay. Bhattacharyya PK et al, had similar cases (65.4% and 77.9%) of organ dysfunction in medical ward and ICU patients respectively.<sup>16</sup> Out of 62 males, 47 (75.80%) had organ dysfunction and of 38 females, 30 (78.94%) had organ dysfunction. Organ dysfunctions in males were highest with 16% in 16-25 years of age group followed by 36-45 years (10%). In females organ dysfunction was



highest in 26-35 years (09%) followed by 46-55 years (08%) group.

Among patients with organ dysfunction, cardiovascular dysfunction was found to be most common with 50 (64.93%), followed by renal 48 (62.33%), respiratory 31 (40.25%), G.I. system 18(23.37%) and hematological 18 (23.37). Umegaki T et al, had 73% cardiovascular, 69.4% respiratory and 39% renal dysfunction, whereas Desai SR et al, found 80% involvement of respiratory system and 58% dysfunction of cardiovascular system.<sup>25,22</sup> Cardiovascular system involvement was present in 27 (75%) cases of pneumonia, 12 (63.15%) cases of malaria, 2 (10.52%) cases of UTI, 5 (45.45%) cases of Meningoencephalitis and 4 (26.66) cases of unspecified infection. Renal dysfunction was present in 10 (27.77%) cases of pneumonia, 16 (84.21%) cases of malaria, 11 (57.89%) of UTI, 4 (36.36%) cases of Meningoencephalitis and 7 (46.66%) cases of unspecified infection.

Out of 77 cases of organ dysfunction, 31 (40.25%) had more than two organ dysfunction with 25 (80.64%) death and 24 patients had one organ dysfunction with only 1 (4.16%) death. Mortality was higher with increase no of organ dysfunction. This is similar to the result observed by Bhattacharya PK et al.<sup>16</sup>

Combination of cardiovascular and renal involvement was maximum (32%) followed by respiratory and cardiovascular and G.I. and renal combination involvement, which are 29% and 17% respectively.

Among the different age group of patients, maximum death was within 56-65 years (54.54%) and minimum mortality was noticed within the age group of 46-55 years (23.07%). Overall mortality was found to be 38%. Bhattacharya PK et al, found 32% mortality among patients in the medical ward.<sup>16</sup> There was a rise in mortality in patients with advanced age with associated multi-organ dysfunction. Studies from various part of the world show mortality due to sepsis in the range of 50-60%.<sup>26,9</sup>

In present study, 26 patients had co-morbid conditions; out of which diabetes mellitus was the most common (13) co-morbidity with 8 (61.53%) patients had organ dysfunction. Bhattacharya PK et al and Martin GS et al also found diabetes mellitus as the most common co-morbid condition in their studies.<sup>16,27</sup> Mortality in this group was found to be 5 (27.7%), where as it was 100% in co-morbid conditions like CML, CKD and Rheumatoid arthritis.

In this study, mean APACHE II score of all the studied patients was 14.87. The mean APACHE II score was high among the death cases than survivors (22.55 v/s 10.16).

So far as the interventional modalities are concerned, 31 cases were mechanically ventilated and 24 (77.4%) patients died. Out of the 28 patients of renal replacement therapy, 9 (32.1%) cases died. 27 cases were given vasopressors support and 21 (77.8%) died. In a study conducted by Desai SR et al, out of 38 patients who were mechanically ventilated, 24 (63.15%, n=38) cases died.<sup>22</sup> They also reported 8 cases of renal replacement therapy with 4 (50%) death.

## CONCLUSION

Pathophysiology of sepsis is complex and multifactorial. In severe cases sepsis can lead to septic shock, widespread organ failure and death. In this study no of females are less than males but organ dysfunction and mortality are more in females. Pneumonia was the most common source of infection. Cardiovascular system was the commonest organ dysfunction. Mortality was highest among multi-organ dysfunction. Most of the patients had APACHE II score >17. So, presence of organ dysfunction has an impact on severity and outcome of sepsis. Increase in no of organ dysfunction affects prognosis and decreases survival.

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