A single centre experience with CytoSorb® as an adjunct therapy in critically ill patients with sepsis: a case series

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ABSTRACT — OBJECTIVE: **Sepsis is an immune response to infections that are caused by bacteria, viruses, fungi, or parasites. This potentially life-threatening condition is associated with high mortality and morbidity that causes a major global health burden and hence requires intense therapeutic support and close monitoring. As a result, substantial work has been done to enhance outcomes by focusing on alternate treatment strategies. One such approach is CytoSorb®, an extracorporeal blood purification therapy that is used for elevated cytokines levels in patients admitted to ICU suffering from sepsis and septic shock, cytokine release syndrome, COVID-19, ARDS, etc. We present authors' experience of using CytoSorb® therapy as an adjuvant in six critically ill patients from India with sepsis or septic shock.**

PATIENTS AND METHODS: **In this case series, we report the outcomes of six severely ill Indian adults with sepsis or septic shock who were treated by CytoSorb® as an adjuvant therapy.**

RESULTS: **All patients across wide age groups demonstrated significantly reduced inflammatory mediators and vital parameters when CytoSorb® therapy was initiated within 24 hours of admission in ICU. It was also found to be effective and safe in patients with COVID-19 and associated post-COVID symptoms. The present case series showed rapid hemodynamic stability and enhanced survival in all patients except one, as a consequence of hemoadsorption utilizing CytoSorb®, especially in individuals for whom therapy was initiated early.**

CONCLUSIONS: **CytoSorb® treatment is efficient in cases where elevated levels of cytokines lead to hyperinflammation. It not only resolves excessive inflammation, but also improves organ dysfunction and provides further clinical benefits in severely ill patients.**

KEYWORDS
Sepsis, septic shock, Covid-19, CytoSorb®.

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INTRODUCTION

Sepsis is defined as the host's dysregulated inflammatory response to an infection causing life-threatening organ dysfunction. It involves physiological, biochemical, and pathological peculiarities that cause mortality and morbidity among patients in the intensive care unit (ICU)[1]. Despite the significant advances in medical treatment, ventilator management, antibiotic therapy, and resuscitative strategies[2], sepsis remains the most common cause of death in ICU[3]. As of 2020, more than 49 million cases of sepsis were reported globally; among these, 11 million deaths were due to sepsis, accounting for approximately 19.7%. It has been estimated that the cost of medical care associated with sepsis is more than $24 billion annually in the US alone[4].

Clinical manifestations of sepsis start with inflammation and can develop to circulatory organ dysfunction associated with significant haematopathological changes. Consumptive thrombocytopenia, vascular microthrombosis[5], multiple organ dysfunction syndromes (MODS)[6], septic shock, and coagulopathy[7] are well-defined clinical manifestations of sepsis. Other features include fever, leukocytosis, respiratory failure, increased heart rate, and hypotension[8]. Notably, these clinical features of sepsis are also common to the Coronavirus 2019 (COVID-19)[9]. Also, COVID-19 is associated with a cytokine storm that demonstrates the beginning of the sepsis process involving to elevated pro-inflammatory and anti-inflammatory cytokine levels[10]. To eliminate the cytokine storm and sepsis, the conventional treatment approach includes vasopressor therapy, mechanical ventilation support, renal replacement therapy and appropriate antibiotic therapy[11]. CytoSorb®, an European CE mark approved and ISO certified hemoadsorption device, is the recent advancement in the management for sepsis and septic shock that is used to eliminate cytokines from the body[12]. It has been proposed as an adjunctive therapy that reduces the excess inflammatory mediators in the blood of critically ill patients with septic shock[13,14] which could weaken the immense inflammatory response associated with sepsis and hence limit the incidence of developing multi-organ failure[15]. It is used worldwide for all indications with elevated cytokines levels (Intended Use) in ICU patients suffering from sepsis and septic shock, COVID-19, cytokine release syndrome, acute respiratory distress syndrome (ARDS), liver failure, influenza and trauma[16]. Also, the therapy could be an alternative therapy to be used as an adjuvant in the hyper-cytokinemic state in patients with chronic kidney disease (CKD) caused due to septic shock and other secondary causes[17]. The therapy has also showed remarkable improvement in patients during emergency cardiac surgery treated with anti-platelet agents. The therapy helped in reducing the risk of bleeding complications, thereby improving outcomes[18]. CytoSorb® is also approved for Emergency Use by the Food and Drug Administration (FDA) for COVID 19[19]. In this case series, we present authors' experience of using CytoSorb® therapy as an adjuvant in six critically ill patients from India with sepsis or septic shock. Al

l patients except one showed a speedy recovery and were discharged in a stable condition from the hospital.

CASE PRESENTATION

Patient 1

A 15-year-old female diagnosed with diabetic ketoacidosis (DKA), seizures, severe metabolic acidosis, septic shock, right-sided acute ischaemia, compartment syndrome of right femoral, popliteal, artery embolectomy and ampulla, with a medical history of diabetes, was admitted to ICU on May 31, 2021. Her demographic details and clinical conditions were recorded by the hospital (Table 1). During the initial physical examination, a body temperature of 37°C, heart rate of 151 beats/min, respiratory rate of 26 breaths/minute, and blood pressure of 165/98 mmHg were observed. Haemoglobin (14 g/dL), total leucocytes count (TLC) (17400 /mm^3), platelets (4800 cells/ml), serum creatinine (1.11 mg/dL), serum glutamic-oxaloacetic transaminase (SGOT) (21.1 units/L), serum glutamic pyruvic transaminase (SGPT) (20.1 units/L), sodium (150 mEq/L), potassium (3.84 mEq/L) and Procalcitonin (PCT) (2.36 ng/ml) were measured (Table 2). Intravenous antibiotics (Zostum, Mero and Tigecycline) and other drugs such as Ecosprin were also given to the patient. The patient's condition was indicative of sepsis and septic shock; CytoSorb® therapy was initiated on June 1, 2021 post 24 hrs of admission in ICU.

CytoSorb® adsorber (3 devices in total, 16 hrs each) was commenced with haemodialysis (HD) (aPTT 31.34 seconds and ACT 31.30 seconds). An improvement in the clinical parameters was observed post-CytoSorb® therapy, with a reduction in TLC, platelet counts, SGPT and PCT levels by 41%, 58%, 67% and 35%, respectively compared to the baseline. Her heart rate (110 beats/min) and blood pressure (120/90 mmHg) also ameliorated after CytoSorb® therapy. She recovered post CytoSorb® therapy and her antibiotics were switched to Tigecycline, Zostum and Colistin and other drugs, Pantocid, Somatostatin, Caspofungin. After 22 days, the patient was discharged in

Table I. Patients' Demographic, Clinical Characteristics, Drugs Associated, and Outcome.

S.no	Age (years)/ Sex	Medical History	Comorbidities	Drugs (pre-CytoSorb)	Drugs (post-CytoSorb)	Outcomes
1.	15/F	Diabetes	DKA, septic shock, seizures, right sided acute ischaemia, compartment syndrome of right femoral, popliteal, artery embolectomy and ampulla	Zostum Tigecycline Ecosprin Mero	Zostum Tigecycline Colistin Pantocid, Somatostatin, Caspofungin	Survived
2.	47/ M	Cardiovascular stroke Right hemi-maxillectomy	Tachypnea, post- COVID-19 mucomycosis, AKI, hypotension	Teicoplanin Meropenem	Amphotericine[b]	Survived
3.	61/F	Hypertension Diabetes	Left side flank pain, vomiting left ureteric stone, septic shock, MODS, AKI and ischaemic heart disease			Survived
4.	30/M	CKD Hypertension	COVID19-positive, acute viral pneumonia	Azee, Doxy, Cefereidone Renopress, Nicardia Renolog	Remdesivir	Survived
5.	70/F	Urosepsis AKI Hypertension Morbid obesity	Coryza, sneezing, vertigo, tachypnea, tachycardia, AKI	Meropenem Poly B Fluconazole Targocid	Feronem, Linezolid, Levoflox	Survived
6.	48/M	Macrophage activation syndrome, MODS, diabetes and hypothyroidism	Hearing loss, generalised weakness and weight loss, tachypnea, hypotension	Merocit Teicoplanin Poly B Caspofungin	Dobutamine Vasopressin	Not Survived

Abbreviations: DKA- Diabetic ketoacidosis; AKI- Acute Kidney Injury; CKD- Chronic Kidney Disease; MODS- Multiple Organ Dysfunction Syndrome .

CLINICALLY STABLE CONDITION

Patient 2

A 47-year-old male with a six-year-old medical history of cardiovascular stroke was admitted to the emergency room. He had a right hemi-maxillectomy performed two weeks before admission. His demographic details and clinical conditions were recorded by the hospital (Table 1). The patient was diagnosed with post-COVID-19 rhino-sinus mucormycosis, tachypnea (42 breaths/min), acute kidney injury (AKI-creatinine >3 mg/dl)) and hypotension (70/40 mmHg) with oxygen saturation (SpO_2) 96% on room air. The arterial pH, bicarbonate, partial pressure of carbon dioxide (pCO_2), partial pressure of oxygen (pO_2) and total carbon dioxide (tCO_2) of the patient were 7.40, 16.4 mmol/L, 26.3 mmHg, 82 mmHg, and 14.6 mmol/L, respectively. Due to reduced oxygen capacity, non-invasive Biphasic Positive Airway Pressure (BiPAP) therapy was commenced. Considering the ongoing hypotension, he was placed on vasopressin therapy and norepinephrine. In addition, intravenous antibiotic therapy including Teicoplanin (twice daily on the first day and daily thereafter) and Meropenem (three times daily) were administered to the patient. TLC (42,280/ mm^3), serum creatinine (3.58 mg/dL), C-reactive protein (CRP) (226 mg/L), and PCT (100 ng/ml) were recorded which corroborated a severe systemic hyperinflammatory state, associated with cytokine release syndrome that could develop into septic shock (Table 2). Despite giving the best standard therapeutic measures, the patient's clinical conditions kept on deteriorating. Thus, CytoSorb® adsorber (one adsorber placed pre-dialyser for 16 hours, flow rate: 200 ml/min, heparin: 200 IU and aPTT: 50 seconds) was integrated into the haemodialysis (HD) machine. Post-CytoSorb® therapy, the patient was haemodynamically stabilised (blood pressure 120/82 mmHg) with reduced CRP (88%), serum creatinine (34%) and improved oxygenation (376 mmHg) throughout 5 days, the blood pressure was maintained and vasopressors were weaned off. As there was a major improvement in his oxygenation (pO2-376 mmHg), oxygen therapy was gradually weaned off. After 9 days from his initial admission, the patient was discharged in a clinically stable condition from the hospital. He was administered a broad-spectrum antifungal drug (Amphotericin b) to be continued until complete resolution of the mucormycosis infection.

Table II. Effect of CytoSorb® Device on Various Values of Biomarkers.

Normal range		Parameters							
		PCT (ng/ml) <0.1 ng/ml	TLC (10^3/ml) 4000-11,000/µL	Platelets (10^3/ml) 50-400,000/mm^3	CRP (mg/L) <10 mg/L	Lactate (mg/dl) Venous: 4.5-19.8 Arterial: 4.5-14.4 mg/dl	Haemo-globin (g/dl) Men:13.2-16.6 g/dl Women: 11.6-15 g/dl	Serum creatinine (mg/L) Men: 0.74 - 1.35 mg/dL Women: 0.59-1.04 mg/dL	IL-6 (pg/ml) 0-43.5 pg/ml
Patient 1	Pre-CytoSorb	2.36	17.4	4.8	20.1		14	1.11	
	Post-CytoSorb	1.53	10.2	2.03	12		8.4	2.19	
Patient 2	Pre-CytoSorb	100	4.2		226			3.58	
	Post-CytoSorb				27.8			2.38	
Patient 3	Pre-CytoSorb	68.19	12.18	187	6.17	6.35	7.4	1.12	
	Post-CytoSorb	35.45	10.48	401.6	80.14	6.38	10.3	1.43	
Patient 4	Pre-CytoSorb		3.8	1.85			10	3.6	
	Post-CytoSorb		24.6	2.14			7.3		
Patient 5	Pre-CytoSorb	172.53	28.19	1.97	50.21		9.6	2.03	4519
	Post-CytoSorb	42	18.21	1.72	51.18		9.3	1.64	532
Patient 6	Pre-CytoSorb	1.33	84	59	230.6		7.2	0.7	
	Post-CytoSorb	6.12	49	38			9	0.4	

Patient 3

A 61-year-old female with a history of hypertension and diabetes was admitted to the hospital on December 30, 2020. Her demographic details and clinical conditions were recorded by the hospital (Table 1). She had the complaints of left sided flank pain directing from the back, and was diagnosed with a left ureteric stone, vomiting, septic shock, multiple organ dysfunction syndrome (MODS), and AKI and ischaemic heart disease. Initial vital signs revealed a respiratory rate of 18 breaths/min, SpO_2 of 98% on room air and blood pressure of 130/90 mmHg. On January 10, 2021, the patient's glycated hemoglobin (HbA1c) was 6.43%, TLC was 14,180/mm^3, CRP was 6.17 mg/L and troponin I was 24.5 ng/L (Table 2). His clinical condition worsened, and he was admitted to ICU. Within 24 hours of admission to ICU, CytoSorb® therapy was started as the patients was in septic shock (with AKI and MODS) with a single device (aPTT: 27 seconds). Post-CytoSorb® therapy, the laboratory parameters showed an improvement from the baseline with a decrease in TLC (26%), PCT (48%) and potassium (9%) levels and an increase in haemoglobin (39%) levels. Within 24 hours of CytoSorb® therapy, her condition was haemodynamically stable. The patient was discharged after 20 days from the initial admission to the hospital.

Patient 4

On December 6, 2020, a 30-year-old male with a medical history of chronic kidney disease (CKD) and hypertension was admitted to the hospital. He was confirmed to be COVID-19-positive with symptoms of acute viral pneumonia. The patient's demographic details and clinical conditions were recorded by the hospital (Table 1). His body temperature (36°C), heart rate (100 beats/min), respiratory rate (20 breaths/min), urine output (200 ml/day) and blood pressure (120/80 mmHg) were recorded at time of admission. The patient was given antibiotics (Azee, Doxy, and Cefereidone), anti-hypertensive drugs (Renopress, Nicardia) and medication for CKD (Renolog). Blood reports revealed the reduced levels of haemoglobin (10 g/dl), TLC (3800 cell/µL), platelet count (1.85x10^3/ml) and slightly increased serum creatinine (3.6 mg/L) (Table 2**)**. Based on the clinical findings, the patient was admitted to ICU on December 8, 2020 and a treatment protocol devised. CytoSorb® therapy (two devices for 16 hrs each with a flow rate of 1220/520) was initiated 2 days later. Post-CytoSorb® therapy, an increase of 547%, 16% and 67% in TLC, platelet count and serum creatinine level were respectively observed. Additional dialysis was performed on December 12, 2020. The patient stabilised and improved clinically. All the drugs were stopped except Remdesivir. He was discharged in a stable condition from the hospital on December 13, 2020.

Patient 5

A 70-year-old female with a history of hypertension, diabetes, morbid obesity and complaints of sneezing and coryza (past 14 days), vertigo and decreased urine output (past 1day) was admitted to the hospital on August 20, 2020. Her demographic details and clinical conditions were recorded by the hospital **(**Table 1**).** On examination, she had urosepsis, tachypnea (30 breaths/min), tachycardia (120 beats/min), AKI and hypertension (140/90 mmHg). Laboratory tests showed an increased TLC (24570/mm^3), serum creatinine (2.03 mg/L), Interleukin - IL-6 levels (4579 pg/ml), hyperkalaemia (6.06 mEq/L), PCT (>100 ng/ml) and altered electrolytes (Table 2**)**. Based on these blood results, she was admitted to ICU on August 21, 2021. The patient was managed with BiPap, intravenous antibiotics (Targocid, Meropenem, Poly-B), low molecular weight heparin (LMWH), nebulisations and other drugs. CytoSorb® therapy was started within 24 hours of admission to the ICU. Post-CytoSorb® therapy, an improvement in the vital parameters including a reduction in TLC (35%), platelet count (13%), PCT level (76%), serum creatinine (19%) and potassium (29%) was observed. The patient was discharged in a stable condition on August 24, 2021. The patient was given intermittent BiPAP support, glucose levels were managed, the Foley catheter was removed and she was able to pass the urine freely. She was discharged in a haemodynamically stable condition after 9 days in the hospital. The patient was further advised to continue BiPAP (twice a day), and medications (including Feronem, Linezolid, Levoflox) for further 3 weeks, to check fasting and post-prandial blood sugar levels every alternate day at home and to follow up in the Out Patient Department (OPD).

Patient 6

A 48-year-old male with complaints of hearing loss (past 7 days), weight loss and generalised weakness (for the previous 2 months) and a medical history of macrophage activation syndrome, MODS, diabetes and hypothyroidism was admitted to the hospital. On November 27, 2020, due to sudden breathlessness (30 breaths/min), SpO_2 of 94% on room air, high heart rate (120 beats/min) and hypotension (110/70 mmHg), he was admitted to ICU and was immediately given BiPAP support. The patient's demographic details and clinical conditions were recorded by the hospital (Table 1). Due to his clinical state including oliguria and hypotension, he was intubated and ventilated, and given inotropic support. Reduced TLC (840 cells/mm^3), platelet count (59000 cells/ml) and elevated inflammatory markers indicated increased infection (Table 2**)**. He was managed with a mechanical ventilator, an-

tibiotics (Merocit, Teicoplanin, Poly-B) and antifungal drugs (Caspofungin) appropriately. However, he was anuric and his condition deteriorated further; so, it was decided to start HD dialysis with CytoSorb® adsorber (16 hours duration) within 24 hours of this admission to the ICU. Post-CytoSorb® treatment, he showed a mild improvement in his laboratory tests with increased haemoglobin (25%) and reduced TLC (42%), platelet count (55%), and serum creatinine (43%). The patient was given an intravenous injection (dobutamine) to treat the weakened heart muscle and started vasopressin to try and improve urine production, and the persistent hypotension. His vital parameters continuously dropped including pCO_2 (28.4 mmHg), pO_2 (148.7 mmHg) and tCO_2 (19 mmol/L). On November 30, 2021, the patient developed bradycardia with high positive end-expiratory pressure (PEEP), hypoxia and hypotension. Emergency drugs and cardiopulmonary resuscitation (CPR) were given for 30 minutes; however, unfortunately, the patient was not revived and was declared dead on November 30, 2021.

DISCUSSION

Sepsis is a common life-threatening condition, and is one of the leading causes of death in ICU[20,21]. It is associated with effects on primary and secondary immune tissues, endothelial tissues, parenchymal tissues, the microcirculation, and coagulation[22]. The mortality rate is usually high for severe sepsis and sepsis shock ranging from 18% and 50%[23]. In the present study we evaluated the use of CytoSorb® therapy concerning clinical outcomes in six critically ill patients with sepsis or septic shock. CytoSorb® haemoadsorption device can be inserted either into a dialyser or used as a standalone. It is a detoxification system which is usually used to reduce the excess levels of several mediators with the aim to control the cytokine storm[14]. In the present case series, CytoSorb® therapy is utilized to manage the critically ill patients. The therapy has proved to significantly reduce the inflammatory mediators and vital parameters (Table 2**)**.

A recent study conducted in patients with sepsis reported that a significant decrease in PCT was observed post-CytoSorb® therapy (p=0.004)[24]. Another study reported marked reduction in CRP (27%) and PCT (65%) levels in patients with sepsis after CytoSorb® therapy (16). A previous study conducted in 135 patients with severe sepsis showed a significant reduction in IL-6 and PCT levels post CytoSorb® treatment[25]. Similar observations were made in our study where a reduced CRP and PCT levels were observed post-CytoSorb® treatment.

In addition, CytoSorb® therapy can provide maximum benefit if the therapy is applied early in the treatment course especially within 24 hours of admission in ICU and for an adequate duration until haemodynamic stability in the patient is achieved[19,26]. In the present study, the patients (except patient 6) achieved clinical stabilisation after the early use of CytoSorb® therapy. Even patient 6 demonstrated mild improvements in haemodynamics after early use of CytoSorb® therapy; however, none of the medical treatments would have helped the patient to survive given that his condition was very critical. Several studies have demonstrated CytoSorb® to be a rescue adjuvant therapy to treat critically ill patients in all age groups ranging from 1 month to 80 years[27,28]. In the current study, CytoSorb® therapy was used in patients with a wide range of ages (15 years to 70 years). As of 2021, CytoSorb® therapy has been used to treat over 5,750 critically ill patients infected with COVID-19 in 30 countries[29], with sepsis the primary cause of most deaths in COVID-19 patients[30]. A clinical trial in COVID-19 patients in the ICU with CytoSorb® is ongoing and expected to be completed by November 2022(NCT04391920)[31]. Wunderlich et al[32] observed in a case series of 13 patients with COVID-19 related ARDS treated with CytoSorb® therapy, a significant decrease in CRP as compared with baseline. Another study conducted in a patient with COVID-19 reported a reduction in CRP values from 1,040pg/ml to 415 pg/mL post-CytoSorb® therapy[33]. In the present case series, a reduction of 88% in CRP level was observed after CytoSorb® therapy in patient 2 with post-Covid complications.

In addition, the most studied inflammatory biomarker is PCT in sepsis and the degree of induction of PCT is associated with the presence of organ dysfunction and severity of septic infection[34]. This study also reported that the average serum PCT levels were four-times higher in severe patients and were eight-times higher in critical patients compared to moderate COVID-19 patients[35]. Moreover, an increased level of PCT can mark the initiation of CytoSorb® therapy[36]. Similar observation was made, and therapy was initiated in patients 1, 2, 3 and 5, where baseline PCT levels were 2.36 ng/ml, 100 ng/ml, 68 ng/ml and 178 ng/ml, respectively (Table 2**).**

CONCLUSIONS

The present study describes the experiences of the authors for the effectiveness and safety of CytoSorb® therapy in six critically ill patients within a wide age range. It is also effective in patients with COVID-19 and associated post-COVID-19 symptoms. CytoSorb® treatment efficiently resolves/ modulates hyperinflammation by removing elevated levels of cytokines. This further improves organ dysfunction and provides clinical stability with no serious adverse effects. When initiated early after admission to ICU, CytoSorb® therapy can be a potential rescue therapy in severely ill patients.

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Ethics approval:
As this is a retrospective case series and all patient data were de-identified, the authors didn't require additional intervention or contact with the patients after their treatment. The intervention (CytoSorb) had already been screened and approved by the hospital authorities at the time of treating the patient.

Informed consent:
Patients gave their consent for treatment during their admission and subsequent stay at the hospital. No additional approvals or consent were sought for this case series.

Availability of data and materials:
The data that support the findings of this study are available from the corresponding author, [HG], upon reasonable request.

Conflict of interests:
The authors have no conflict of interest to declare

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References

1. Huang M, Cai S, Su J. The pathogenesis of sepsis and potential therapeutic targets. Int J Mol Sci 2019; 20: 5376.
2. Kogelmann K, Jarczak D, Scheller M, Drüner M. Hemoadsorption by CytoSorb in septic patients: a case series. Critical Care 2017; 21: 1-10.
3. Rello J, Valenzuela-Sánchez F, Ruiz-Rodriguez M, Moyano S. Sepsis: a review of advances in management. Adv Ther 2017; 34: 2393-411.
4. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, Colombara DV, Ikuta KS, Kissoon N, Finfer S. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet 2020; 395: 200-11.
5. Chang JC. Sepsis and septic shock: endothelial molecular pathogenesis associated with vascular microthrombotic disease. Thromb J 2019; 17: 1-19.
6. Spapen HD, Jacobs R, Honoré PM. Sepsis-induced multi-organ dysfunction syndrome—a mechanistic approach. J Emerg Crit Care Med 2017; 1: 27.
7. Marcel L, Van der Poll T. Coagulation and sepsis. Thromb Res 2017; 149: 38-44.
8. Gauer RL. Early recognition and management of sepsis in adults: the first six hours. Am Phys 2013; 88: 44-53.
9. Olwal CO, Nganyewo NN, Tapela K, Djomkam Zune AL, Owoicho O, Bediako Y, Duodu S. Parallels in sepsis and COVID-19 conditions: implications for managing severe COVID-19. Front Immunol 2021; 12: 602848.
10. Li H, Liu L, Zhang D, Xu J, Dai H, Tang N, Su X, Cao B. SARS-CoV-2 and viral sepsis: observations and hypotheses. Lancet 2020; 395: 1517-20.
11. Annane D, Aegerter P, Jars-Guincestre M, Guidet B. for the CUB-Réa Network. Current epidemiology of septic shock. Am J Respir Crit Care Med 2003; 168: 165-72.
12. Shum H, Yan W, Chan D. Extracorporeal blood purification for sepsis. Hong Kong Med J 2016; 22: 478-85.
13. Mehta Y, Mehta C, Kumar A, George JV, Gupta A, Nanda S, Kochhar G, Raizada A. Experience with hemoadsorption (CytoSorb®) in the management of septic shock patients. World J Crit Care Med 2020; 9: 1-12.
14. Singh Y, Chhabra S, Lashkari K, Taneja A, Garg A, Chandra A, Chhabra M, Singh G, Jain S. Hemoadsorption by extracorporeal cytokine adsorption therapy (CytoSorb®) in the management of septic shock: A retrospective observational study. Int J Artif Organs 2020; 43: 372-8.
15. Ali J, Vuylsteke A. Extracorporeal membrane oxygenation: indications, technique and contemporary outcomes. Heart 2019; 105: 1437-43.
16. Bonavia A, Groff A, Karamchandani K, Singbartl K. Clinical utility of extracorporeal cytokine hemoadsorption therapy: a literature review. Blood Purif 2018; 46: 337-49.
17. Palevsky PM. Renal replacement therapy in acute kidney injury. Adv Chronic Kidney Dis 2013; 20: 76-84.
18. Kumar N, Keshri V, Bhuyan R. CytoSorb® usage in a dual antiplatelet agent treated patient during CABG and broken guidewire retrieval from right coronary artery ostium. IJMDAT 2022; 5: e379.
19. Ruiz-Rodríguez JC, Molnar Z, Deliargyris EN, Ferrer R. The use of cytosorb therapy in critically ill COVID-19 patients: Review of the rationale and current clinical experiences. Crit Care Res Pract 2021; 2021: 7769516.
20. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche J-D, Coopersmith CM. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016; 315: 801-10.
21. Cecconi M, Evans L, Levy M, Rhodes A. Sepsis and septic shock. Lancet 2018; 392: 75-87.
22. Hotchkiss RS, Moldawer LL, Opal SM, Reinhart K, Turnbull IR, Vincent J-L. Sepsis and septic shock. Nat Rev Dis Prim 2016; 2: 1-21.
23. Andriolo BN, Andriolo RB, Salomao R, Atallah AN. Effectiveness and safety of procalcitonin evaluation for reducing mortality in adults with sepsis, severe sepsis or septic shock. Cochr Syst Rev 2017; 1: CD010959.
24. Hawchar F, Laszlo I, Öveges N, Trasy D, Ondrik Z, Molnar Z. Extracorporeal cytokine adsorption in septic shock: a proof of concept randomized, controlled pilot study. J Crit Care 2019; 49: 172-8.
25. Brouwer WP, Duran S, Kuijper M, Ince C. Hemoadsorption with CytoSorb shows a decreased observed versus expected 28-day all-cause mortality in ICU patients with septic shock: a propensity-score-weighted retrospective study. Crit Care 2019; 23: 1-9.
26. Ankawi G, Xie Y, Yang B, Xie Y, Xie P, Ronco C. What have we learned about the use of cytosorb adsorption columns? Blood Purif 2019; 48: 196-202.
27. Padiyar S, Deokar A, Birajdar S, Walawalkar A, Doshi H. Cytosorb for management of acute kidney injury due to rhabdomyolysis in a child. Indian Pediatr 2019; 56: 974-6.
28. Bottari G, Confalone V, Cotugno N, Guzzo I, Perdichizzi S, Manno EC, Stoppa F, Cecchetti C. Efficacy of CytoSorb in a pediatric case of severe multisystem infammatory syndrome (MIS-C): a clinical case report. Front Pediatr 2021; 9: 676298.
29. Cytosorbents Corporation, CytoSorb Literature Database, 2018. https://literature.cytosorb.com. Accessed 11-nov-2022.

30. Beltran-Garcia J, Osca-Verdegal R, Pallardo FV, Ferreres J, Rodriguez M, Mulet S, Ferrando-Sanchez C, Carbonell N, Garcia-Gimenez JL. Sepsis and coronavirus disease 2019: common features and anti-inflammatory therapeutic approaches. Crit Care Med 2020; 48: 1841-1844.
31. Zothantluanga JH, Lalthanzara H, Shakya A, Chetia D. The outbreak of Covid-19 in Mizoram, India. Rizug 2020.
32. Wunderlich-Sperl F, Kautzky S, Pickem C, Hörmann C. Adjuvant hemoadsorption therapy in patients with severe COVID-19 and related organ failure requiring CRRT or ECMO therapy: a case series. Int J Artif Organs 2021; 44: 694-702.
33. Berlot G, Tomasini A, Pognuz ER, Randino A, Chiella F, La Fata C, Piva M, Amato P, Di Maso V, Bianco F. The combined use of tocilizumab and hemoadsorption in a patient with SARS-COV-2-19-associated pneumonia: a case report. Nephron 2020; 144: 459-62.
34. Huang MY, Chen CY, Chien JH, Wu KH, Chang YJ, Wu KH, Wu HP. Serum procalcitonin and procalcitonin clearance as a prognostic biomarker in patients with severe sepsis and septic shock. BioMed Res Int 2016; 2016: 1758501.
35. Hu R, Han C, Pei S, Yin M, Chen X. Procalcitonin levels in COVID-19 patients. Int J Antimicrob Agents 2020; 56: 106051.
36. Ahmed S, Jafri L, Hoodbhoy Z, Siddiqui I. Prognostic value of serum procalcitonin in COVID-19 patients: a systematic review. Indian J Crit Care Med 2021; 25: 77.