ORIGINAL RESEARCH PAPER
Volume - 15 | Issue - 08 | August - 2026 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

RESUSCITATING SHOCK BEYOND BLOOD PRESSURE: LACTATE CLEARANCE, FLUID RESPONSIVENESS, AND VASOPRESSOR PATTERNS IN A MULTIDISCIPLINARY ICU

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ABSTRACT

Introduction: Shock resuscitation requires rapid restoration of tissue perfusion while avoiding unnecessary fluid loading and excessive vasopressor exposure. In Indian intensive care units, heterogeneous case mix, delayed referral, restricted monitoring resources, and variable access to advanced hemodynamic technologies complicate individualized treatment. Integrating serial lactate clearance with a simple dynamic assessment of fluid responsiveness may provide a pragmatic framework for guiding fluids and vasoactive support. **Aim:** To evaluate lactate clearance, dynamic fluid responsiveness, vasopressor strategies, and their associations with short-term outcomes among adults with shock admitted to a multidisciplinary intensive care unit. **Methodology:** A hospital-based prospective observational cohort study included a time-bound consecutive sample of 150 adults with shock admitted to a tertiary-care multidisciplinary ICU. Patients with pregnancy, treatment limitation at admission, advanced liver disease interfering with lactate interpretation, chronic dialysis dependence, or inadequate serial measurements were excluded. Lactate was measured at baseline and six hours; clearance ≥20% was considered adequate. Before any additional study-recorded fluid bolus, fluid responsiveness was assessed using passive leg raising with a ≥10% increase in stroke volume or cardiac output. Fluid exposure, vasopressor requirement and strategy, SOFA score, ventilation within 24 hours, acute kidney injury, ICU stay, and hospital mortality were recorded. Welch's t-test and Fisher's exact test were used for exploratory comparisons. **Results:** Of 150 patients, 105 (70.0%) had septic shock. Fluid responsiveness was present in 89 (59.3%); responders received less crystalloid during the first six hours than non-responders (1.85 ± 0.62 vs 2.54 ± 0.78 L; $p<0.001$) and less frequently required ongoing vasopressors at 24 hours (42.7% vs 67.2%; $p=0.005$). Adequate six-hour lactate clearance occurred in 92 (61.3%). Among initially treated patients, adequate clearance was associated with more frequent vasopressor liberation by 24 hours (52.8% vs 15.1%; $p<0.001$), lower acute kidney injury (20.7% vs 39.7%; $p=0.015$), and lower hospital mortality (19.6% vs 43.1%; $p=0.003$). Among 125 vasopressor-treated patients, norepinephrine monotherapy was used in 75 (60.0%); combination therapy identified a higher-risk subgroup with greater mortality. **Conclusion:** Adequate lactate clearance and dynamic fluid responsiveness were associated with lower treatment intensity and more favourable short-term outcomes. A combined bedside strategy may support individualized resuscitation, although causal benefit requires confirmation in controlled studies.

KEYWORDS

INTRODUCTION

Shock is a time-critical syndrome of acute circulatory failure in which oxygen delivery becomes inadequate for cellular requirements, leading to tissue hypoperfusion, metabolic dysfunction, organ injury, and death. Although hypotension is a conspicuous clinical feature, a blood pressure target alone does not establish restoration of microcirculatory flow or cellular oxygen utilization. The contemporary definition of septic shock incorporates vasopressor dependence and hyperlactatemia because these variables identify a subgroup with particularly high mortality [1]. Across shock phenotypes, effective resuscitation therefore requires simultaneous attention to macrocirculation, peripheral perfusion, biochemical evidence of oxygen debt, and the patient's response to each intervention [2].

Intravenous crystalloid remains an essential initial therapy when reduced effective circulating volume contributes to shock. Nevertheless, the relationship between administered volume and improved cardiac output is inconsistent. Once the ascending portion of the Frank–Starling curve has been exhausted, further fluid may increase venous pressures and interstitial edema without materially improving forward flow. Pulmonary edema, abdominal congestion, renal venous hypertension, impaired tissue oxygen diffusion, and prolonged mechanical ventilation are clinically important consequences of indiscriminate fluid loading. The Surviving Sepsis Campaign recommends initial crystalloid resuscitation while emphasizing frequent reassessment and the preferential use of dynamic rather than static variables to guide additional fluid [3].

Serum lactate is an accessible global marker used to identify severe illness and follow resuscitation. Hyperlactatemia in shock may reflect tissue hypoxia, adrenergic stimulation, impaired hepatic clearance, mitochondrial dysfunction, or combinations of these mechanisms. Consequently, a single concentration is neither a pure measure of anaerobic metabolism nor a direct mandate for additional fluid. Serial change provides more information. Lactate clearance describes the proportional reduction from an initial value and can serve as a pragmatic marker of improving perfusion and metabolic recovery. The ANDROMEDA-SHOCK trial demonstrated that peripheral perfusion–targeted and lactate-targeted strategies can produce different patterns of intervention and organ dysfunction, highlighting the importance of contextual interpretation rather than pursuit of lactate normalization in isolation [4].

Jones et al. showed that lactate-clearance-guided early resuscitation was not inferior to central venous oxygen saturation–guided therapy in severe sepsis and septic shock [5]. Earlier work by Nguyen et al. associated greater lactate clearance with improved outcomes in severe sepsis and septic shock [6]. These findings established serial lactate as a clinically meaningful resuscitation variable; however, lactate kinetics can remain slow despite normalized capillary refill and hemodynamics. Persistent elevation should prompt diagnostic reconsideration, assessment of hepatic function and adrenergic exposure, and evaluation for uncontrolled infection or regional ischemia rather than reflexive fluid administration.

Dynamic assessment of fluid responsiveness provides a complementary physiologic approach. Passive leg raising transiently transfers venous blood toward the central circulation and functions as a reversible internal fluid challenge. When accompanied by real-time measurement of stroke volume or cardiac output, it predicts whether a subsequent bolus is likely to improve flow. A systematic review by Monnet et al. found passive leg raising to be reliable when its effect is assessed by a direct flow variable [7]. The FRESH randomized trial further suggested that passive-leg-raise-guided management can reduce net fluid balance and selected organ-support requirements in septic shock [8]. Dynamic testing is particularly attractive in mixed Indian ICUs because it can be performed repeatedly and does not necessarily require invasive arterial or central venous pressure targets.

Recent fluid trials have reinforced the need for restraint after initial stabilization. The CLASSIC trial compared restricted and standard intravenous-fluid strategies in ICU patients with septic shock and showed that lower fluid exposure was achievable without a clear mortality penalty [9]. CLOVERS compared restrictive and liberal early resuscitation strategies in sepsis-induced hypotension and did not demonstrate superiority of either protocol for mortality before discharge home by day 90 [10]. Together, these studies discourage a universal volume prescription and favour repeated assessment of perfusion, congestion, and fluid responsiveness.

Vasopressors are required when adequate perfusion pressure cannot be maintained with appropriate initial volume restoration. Norepinephrine is recommended as the first-line agent because it raises vascular tone with comparatively limited tachyarrhythmia. Vasopressin may be added when norepinephrine requirements escalate, while epinephrine is generally reserved for refractory shock or selected myocardial dysfunction. In VASST, low-dose vasopressin did not significantly reduce overall mortality compared with norepinephrine but provided important evidence regarding catecholamine-sparing treatment [11]. The VANISH trial similarly examined early vasopressin and kidney outcomes in septic shock without establishing a universal survival advantage [12]. The CENSER trial suggested that earlier norepinephrine can improve early shock control, although its single-centre design and secondary outcomes require cautious interpretation [13].

Indian critical care practice must translate this evidence within substantial heterogeneity of infrastructure and referral patterns. The first Indian Intensive Care Case Mix and Practice Patterns Study documented a high burden of severe sepsis and septic shock and considerable variation across units [14]. The second INDICAPS study confirmed the evolving complexity and mortality of Indian ICU populations [15]. Limited nurse-to-patient ratios, delayed transfer, cost constraints, intermittent access to cardiac-output monitoring, and high prevalence of infection may influence fluid and vasopressor decisions. A pragmatic hospital-based study integrating serial lactate, passive-leg-raise responsiveness, fluid exposure, vasopressor patterns, and patient outcomes may therefore offer locally relevant information. The present study was undertaken to characterize these relationships among adults with shock in a multidisciplinary Indian ICU while maintaining the appropriately non-causal interpretation required by an observational design.

AIM

To evaluate lactate clearance, dynamic fluid responsiveness, vasopressor strategies, and their associations with short-term outcomes among adults with shock admitted to a multidisciplinary intensive care unit.

METHODOLOGY

A hospital-based prospective observational cohort study was conducted in the multidisciplinary adult intensive care unit of a tertiary-care teaching hospital in India from January to December 2025 after Institutional Ethics Committee approval. A time-bound consecutive census of all eligible patients was undertaken, resulting in a final sample of 150 adults. Patients aged 18 years or older with shock at ICU admission or within the first six hours were eligible. Shock was operationally defined as acute circulatory failure with systolic blood pressure <90 mmHg, mean arterial pressure <65 mmHg, a decrease in systolic pressure >40 mmHg from baseline, or vasopressor requirement to maintain mean arterial pressure ≥65 mmHg, accompanied by at least one marker of tissue hypoperfusion such as serum lactate >2 mmol/L, oliguria, altered mentation, cool or mottled extremities, or prolonged capillary refill. Patients who were pregnant, receiving chronic maintenance dialysis, had advanced hepatic failure likely to invalidate lactate kinetics, had an immediate treatment-limitation order, received prolonged resuscitation before transfer without reliable baseline measurements, or lacked either baseline or six-hour lactate and dynamic-flow assessment were excluded. Consecutive sampling was used. Demographic characteristics, comorbidities, referral source, shock phenotype, suspected infection, hemodynamic variables, capillary refill, urine output, arterial blood gas, complete blood count, renal and liver biochemical profiles, microbiological cultures and imaging directed by the suspected source were recorded in a structured case-record form. Septic shock was classified using Sepsis-3 criteria; hypovolemic, cardiogenic, and other distributive or mixed shock phenotypes were adjudicated by the treating intensivist using clinical, electrocardiographic, echo-cardiographic, laboratory, and imaging evidence. SOFA and APACHE II scores were calculated from the first 24 hours. Baseline and six-hour lactate were measured using the same sampling source and analytical platform for each participant. Six-hour lactate clearance was calculated as [(baseline lactate − six-hour lactate)/baseline lactate] ×100; clearance ≥20% was prespecified as adequate. After initial stabilization and before any additional study-recorded fluid bolus, fluid responsiveness was assessed using passive leg raising from a semirecumbent position. Stroke volume or cardiac output was measured continuously with the locally available validated monitor or focused critical-care echocardiography immediately before and during passive leg raising. An increase ≥10% was considered a positive response. Balanced crystalloid was preferred for resuscitation, and additional boluses were determined by perfusion, congestion, and dynamic responsiveness. Norepinephrine was the first-line vasopressor; vasopressin was added for escalating norepinephrine requirements, and epinephrine or another agent was used for refractory shock or a specific physiologic indication. Initial vasopressor requirement was defined as receipt of any vasopressor within six hours of shock recognition. Vasopressor liberation by 24 hours was defined as discontinuation of all vasopressors before 24 hours without reinstitution during the subsequent six hours. Of 125 initially treated patients, 46 met this definition and 79 remained on support at 24 hours. The study was observational and did not mandate treatment. Recorded exposures included crystalloid volume during the first six hours, fluid balance, vasopressor use at baseline and 24 hours, maximum norepinephrine-equivalent dose, and vasoactive strategy. The primary outcome was hospital mortality according to six-hour lactate clearance. Secondary outcomes were vasopressor liberation by 24 hours, change in SOFA score from baseline to 48 hours, invasive mechanical ventilation within 24 hours, KDIGO-defined acute kidney injury during the index ICU admission, ICU length of stay, fluid exposure, and vasopressor strategy. Written informed consent was obtained from the patient or legally authorized representative; confidentiality was maintained and participation did not alter clinical care. Data were analysed using SPSS version 26.0. Distribution was assessed using the Shapiro–Wilk test and visual inspection. Approximately normally distributed continuous variables were expressed as mean ± standard deviation and categorical variables as frequency and percentage. Fluid responders and non-responders and patients with adequate and inadequate lactate clearance were compared exploratorily using Welch's independent-samples t-test for continuous variables and two-sided Fisher's exact test for categorical variables. Vasopressor strategies were summarized descriptively; norepinephrine monotherapy was compared with combination therapy using Fisher's exact test. A two-sided p-value <0.05 was considered statistically significant. Comparisons were prespecified as exploratory and unadjusted, and all findings were interpreted as associations rather than causal effects.

RESULTS

Table 1. Baseline Clinical and Resuscitation Profile of Patients With Shock (n=150)

Variable	Category	n	Percentage / Mean ± SD
Age (years)	Mean ± SD	150	57.2 ± 15.4
Sex	Male / Female	91 / 59	60.7 / 39.3
Shock phenotype	Septic / Hypovolemic	105 / 24	70.0 / 16.0
	Cardiogenic / Other or mixed	15 / 6	10.0 / 4.0
Baseline lactate (mmol/L)	Mean ± SD	150	4.8 ± 1.8
SOFA score	Mean ± SD	150	9.6 ± 3.1
APACHE II score	Mean ± SD	150	20.4 ± 5.7
Initial vasopressor requirement	Required / Not required	125 / 25	83.3 / 16.7
Hospital mortality	Died / Survived	43 / 107	28.7 / 71.3

Interpretation: The cohort had a mean age of 57.2 ± 15.4 years and was predominantly male. Septic shock accounted for 105 cases (70.0%). Baseline lactate and severity scores indicated clinically important hypoperfusion and organ dysfunction; 125 patients (83.3%) required vasopressors, and hospital mortality was 28.7%.

Table 2. Resuscitation Characteristics According to Dynamic Fluid Responsiveness (n=150)

Variable	Fluid responders (n=89)	Non-responders (n=61)	p-value

Proportion of cohort, n (%)	89 (59.3)	61 (40.7)	—
First 6-hour crystalloid (L), mean ± SD	1.85 ± 0.62	2.54 ± 0.78	<0.001†
Ongoing vasopressor use at 24 hours, n (%)	38 (42.7)	41 (67.2)	0.005‡
Invasive mechanical ventilation within 24 hours, n (%)	35 (39.3)	39 (63.9)	0.005‡

Interpretation: Dynamic fluid responsiveness was present in 59.3% of patients. Responders received significantly less crystalloid and less frequently required ongoing vasopressor support at 24 hours or invasive mechanical ventilation within 24 hours. In the complete cohort, 79 patients remained on vasopressors at 24 hours. These associations describe differing physiologic severity and do not establish a treatment effect. †Welch's t-test; ‡two-sided Fisher's exact test.

Table 3. Clinical Outcomes According to Six-hour Lactate Clearance (n=150)

Variable	Clearance ≥20% (n=92)	Clearance <20% (n=58)	p-value
Baseline lactate (mmol/L), mean ± SD	4.6 ± 1.7	5.1 ± 1.9	0.105†
SOFA-score change from baseline to 48 hours, mean ± SD*	−3.1 ± 1.8	−1.2 ± 1.6	<0.001†
Vasopressor liberation by 24 hours among initially treated patients, n/N (%)	38/72 (52.8)	8/53 (15.1)	<0.001‡
Acute kidney injury, n (%)	19 (20.7)	23 (39.7)	0.015‡
Hospital mortality, n (%)	18 (19.6)	25 (43.1)	0.003‡

Interpretation: Adequate six-hour lactate clearance occurred in 92 patients (61.3%). Of the 125 patients initially receiving vasopressors, 72 had adequate clearance and 53 had inadequate clearance; 38/72 (52.8%) and 8/53 (15.1%), respectively, achieved liberation by 24 hours. Thus, 46 patients were liberated and 79 remained on vasopressors at 24 hours. Adequate clearance was also associated with greater SOFA improvement and lower acute kidney injury and hospital mortality. *Negative values indicate improvement; †Welch's t-test; ‡two-sided Fisher's exact test.

Table 4. Initial Vasopressor Requirement, Treatment Strategy, and Hospital Mortality (Full Cohort n=150; Treated Subgroup n=125)

Vasopressor variable	n	Percentage	Hospital mortality, n (%)
No initial vasopressor requirement	25	16.7	6 (24.0)
Initial vasopressor requirement	125	83.3	37 (29.6)
Norepinephrine monotherapy*	75	60.0	14 (18.7)
Norepinephrine plus vasopressin*	35	28.0	15 (42.9)
Norepinephrine plus epinephrine*	10	8.0	6 (60.0)
Other combination strategy*	5	4.0	2 (40.0)
Any combination strategy*	50	40.0	23 (46.0)†

Interpretation: In the full cohort, 125/150 patients (83.3%) required a vasopressor initially and accounted for 37/43 hospital deaths. Within this treated subgroup, norepinephrine monotherapy was used in 75/125 (60.0%), whereas 50/125 (40.0%) received combination therapy. Mortality was higher with combination treatment than with monotherapy (46.0% vs 18.7%; Fisher's exact p=0.001), most plausibly reflecting escalation in refractory shock rather than a causal drug effect. *Percentages use the treated subgroup (n=125) as denominator; †comparison of any combination strategy with norepinephrine monotherapy.

DISCUSSION

The present hospital-based cohort integrated three components of shock resuscitation that are often considered separately: biochemical response assessed by lactate clearance, physiologic response assessed by a dynamic flow test, and the pattern of vasoactive therapy. Septic shock accounted for 70.0% of the 150 patients, with a mean baseline lactate of 4.8 mmol/L and substantial organ dysfunction. This profile resembles the high infection burden described in the first INDICAPS study, in which severe sepsis and septic shock represented a major component of Indian ICU practice [14]. The second INDICAPS study likewise demonstrated substantial illness severity and ICU mortality across Indian units [15]. International early-goal-directed-therapy trials such as ProCESS, ARISE, and ProMISe showed that protocolized invasive targets did not improve survival over contemporary usual care, thereby shifting emphasis toward timely fundamentals and individualized reassessment [16–18]. The baseline pattern in Table 1 is consequently credible for a tertiary Indian referral ICU, although a single-centre sample cannot represent the national case mix.

Dynamic testing classified 59.3% of patients as fluid responsive. Responders received significantly less crystalloid during the first six hours and were less likely to require ongoing vasopressor support at 24 hours or invasive mechanical ventilation within 24 hours than non-responders. These findings do not mean that a positive passive leg raise directly caused improved outcome; rather, preserved preload reserve may identify a more reversible hemodynamic phenotype. Monnet et al. demonstrated that passive leg raising predicts fluid responsiveness reliably when its effect is measured by cardiac output or stroke volume rather than blood pressure alone [7]. In FRESH, Douglas et al. found that passive-leg-raise-guided resuscitation reduced fluid balance and was associated with fewer renal and respiratory support interventions [8]. The present Table 2 is directionally consistent with both reports. It also accords with CLASSIC, which established the feasibility of lower fluid exposure after initial treatment [9], and CLOVERS, which showed no mortality advantage fromimposing a uniformly liberal or restrictive early strategy [10]. The practical message for Indian ICUs is not universal restriction but repeated evaluation of benefit before each additional bolus.

Adequate six-hour lactate clearance occurred in 61.3% of patients. This group showed a larger reduction in SOFA score, more frequent liberation from vasopressors by 24 hours, and lower acute kidney injury and hospital mortality. Nguyen et al. described a strong association between early lactate clearance and survival in severe sepsis and septic shock [6], while Jones et al. demonstrated that lactate-clearance-guided resuscitation was a reasonable alternative to central venous oxygen saturation guidance [5]. The association in Table 3 is therefore biologically and clinically plausible. Nevertheless, baseline lactate did not differ significantly between clearance groups, suggesting that trajectory provided information beyond a single initial concentration. ANDROMEDA-SHOCK further cautions that lactate should be integrated with capillary refill and other perfusion markers, because a peripheral-perfusion-targeted strategy produced less organ dysfunction and a non-significant trend toward lower mortality [4]. In practice, persistent lactate should trigger reassessment of shock source, cardiac output, congestion, adrenergic stimulation, hepatic clearance, and regional ischemia rather than automatic fluid administration.

Vasopressors were required in 125 patients. Norepinephrine monotherapy was the most common strategy, used in 60.0% of treated patients, while vasopressin was the predominant adjunct. Mortality was lower with norepinephrine monotherapy than with any combination strategy; however, this finding is strongly susceptible to confounding by indication because additional agents were used in more refractory shock. The Surviving Sepsis Campaign supports norepinephrine as first-line treatment and suggests vasopressin addition when mean arterial pressure remains inadequate [3]. VASST did not demonstrate a significant overall mortality advantage for vasopressin over norepinephrine, although it established the feasibility of a catecholamine-sparing approach [11]. VANISH likewise did not show a definitive kidney-failure-free survival advantage for early vasopressin [12]. CENSER reported better early shock control with early norepinephrine [13], supporting prompt vasopressor use when hypotension persists rather than delaying treatment for repeated unresponsive fluid boluses. Table 4 should therefore be interpreted as a description of escalating severity, not a comparative-effectiveness analysis of drugs.

The combined findings support a coherent bedside model. Dynamic testing estimates whether a fluid bolus can augment flow; serial lactate helps determine whether the global metabolic trajectory is improving; and vasopressor dose and number reflect the pressure support required while the underlying cause is treated. Discordance is informative. A fluid non-responder with persistent hyperlactatemia should not receive repetitive fluid solely to normalize lactate, whereas a fluid responder with congestion may still require caution. Similarly, a normalized mean arterial pressure with worsening lactate or capillary refill indicates that pressure correction has not necessarily restored effective perfusion. This integrative interpretation is particularly suitable for

resource-variable Indian settings because passive leg raising, serial lactate, urine output, focused echocardiography, and bedside perfusion assessment can be combined without reliance on a single costly platform.

The study has several strengths: prospective consecutive enrolment, prespecified definitions, standardized six-hour lactate clearance, dynamic assessment based on a measured flow response, explicit documentation of crystalloid exposure, and separation of monotherapy from combination vasopressor strategies. The three resuscitation domains were linked to clinically relevant organ-support and mortality outcomes. Important limitations remain. The study was single-centre and descriptive, and the sample of 150 limited precision for uncommon shock phenotypes and vasopressor combinations. Treatment was clinician-directed, creating confounding by severity and indication. Lactate was influenced by mechanisms beyond hypoperfusion, and different locally available devices were used to measure flow. Fluid responsiveness is transient and a positive test does not guarantee that fluid administration is clinically appropriate. The six-hour threshold was prespecified but is not a universal biological boundary. No multivariable adjustment, time-to-event analysis, or external validation was undertaken. Accordingly, the findings should generate locally relevant hypotheses and support structured reassessment; they cannot demonstrate that any resuscitation strategy caused the observed outcomes. Multicentre Indian cohorts and pragmatic trials are needed to test integrated algorithms across different resource settings.

CONCLUSION

Among adults with shock admitted to a multidisciplinary ICU, adequate six-hour lactate clearance and demonstrable dynamic fluid responsiveness were associated with lower subsequent treatment intensity and more favourable short-term outcomes. Norepinephrine monotherapy was the predominant vasoactive strategy, while combination therapy identified patients with more refractory illness and higher mortality. The findings support a pragmatic resuscitation approach that integrates serial lactate with measured flow responsiveness and timely vasopressor escalation rather than relying on blood pressure, lactate, or fluid volume in isolation. Because the study was descriptive and treatment was not randomized, these relationships should be interpreted as markers of physiology and disease severity rather than evidence of causal benefit.

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