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RESEARCH ARTICLE

Correlation Between Serum Biomarkers and Intracompartmental Pressure in Diagnosing Acute Compartment Syndrome in Leg Fractures

Saurabh Jha[1], Shiv Shanker Tripathi[1], Rajiv Ratan Singh[1], Swagat Mahapatra[2], Utkarsh Kumar Srivastava[1], Sachin Kumar Tripathi[3], Pradeep Kumar Yadav[4]

[1]Department of Emergency Medicine, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, India
[2]Department of Orthopaedic Surgery, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, India
[3]Department of Forensic Medicine and Toxicology, King George's Medical University, Lucknow, India
[4]Department of Forensic Medicine and Toxicology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, India

ABSTRACT

Objective: Acute Compartment Syndrome (ACS) is a serious complication of leg fractures that requires timely diagnosis and intervention. While intracompartmental pressure monitoring remains the gold standard for diagnosis, the role of serum biomarkers as non-invasive diagnostic tools is gaining interest. This study investigates the correlation between serum biomarkers and intracompartmental pressure in diagnosing ACS. To evaluate the correlation of serum biomarkers with compartment pressure monitoring in suspected ACS in fractures of the leg and its medico-legal significance.

Materials and Methods: This prospective observational study included 60 patients with leg fractures suspected of developing ACS. Serum biomarkers were measured, including creatine kinase, potassium, lactate, bicarbonate, and chloride. Simultaneously, intracompartmental pressure was recorded using a pressure monitoring device. Data were analysed using descriptive statistics, correlation coefficients, and binary logistic regression to evaluate the association of biomarkers with intracompartmental pressure.

Results: Serum biomarkers, particularly creatine kinase and lactate, offer valuable support in diagnosing ACS in leg fractures, complementing intracompartmental pressure monitoring. Integrating these biomarkers into diagnostic protocols can improve early detection, especially in resource-limited settings. This research underscores the medico-legal significance, as accurate ACS identification prevents legal issues arising from delayed intervention and patient harm.

Conclusion: Serum biomarkers, particularly creatine kinase and lactate, show promise as adjuncts to intracompartmental pressure monitoring for diagnosing ACS in leg fractures. Incorporating these biomarkers into diagnostic protocols may enhance early detection, particularly in resource-limited settings. Further studies are needed to validate these findings and establish clinical thresholds. This research highlights the medico-legal significance of serum biomarkers in diagnosing ACS in leg fractures. Elevated creatine kinase and lactate levels, along with clinical findings, provide crucial evidence for timely diagnosis and treatment. Accurate identification of ACS can prevent legal implications related to delayed intervention and patient harm.

Keywords: Acute compartment syndrome (ACS), diagnostic correlation, intracompartmental pressure, leg fractures, medico-legal implications, serum biomarkers

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INTRODUCTION

Acute compartment syndrome (ACS) stands as a critical orthopaedic emergency characterized by increased pressure within a closed fascial compartment, leading to compromised tissue perfusion and potential neurovascular compromise.[1] This syndrome predominantly manifests in the lower extremities following traumatic injuries such as fractures of the leg. Despite advances in trauma care and surgical techniques, timely diagnosis and management of ACS remain formidable challenges, necessitating the ex-

Address for Correspondence: Saurabh Jha, Department of Emergency Medicine, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, India
E-mail: dctrprdp@gmail.com **ORCID ID:** 0009-0004-7296-202X

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ploration of novel diagnostic modalities and biomarkers to aid in its early detection and intervention.[2] In the clinical milieu, the gold standard for diagnosing ACS has been intra-compartmental pressure monitoring, although its invasiveness and limitations have spurred interest in identifying serum biomarkers that may serve as adjuncts or alternatives in ACS diagnosis.[3] Recent research has emphasized the exploration of various biochemical markers indicative of tissue ischemia, inflammation, and cellular damage associated with compartmental pressure elevation. Among these biomarkers, CK, myoglobin, and interleukin-6 (IL-6) have garnered significant attention for their potential utility in aiding ACS diagnosis and prognostication.[4] This research paper aims to investigate the correlation between serum biomarkers and intracompartmental pressure monitoring in clinically suspected cases of ACS secondary to leg fractures. By elucidating the relationship between these biomarkers and intracompartmental pressures, we aim to enhance diagnostic accuracy and expedite the management of ACS, thereby mitigating the associated morbidity and improving patient outcomes. ACS stands as a grave condition characterized by increased pressure within a closed anatomical compartment, leading to compromised tissue perfusion and potential neurovascular compromise.[5] Despite advancements in medical knowledge and surgical techniques, ACS remains a significant concern, particularly in trauma and orthopaedic settings.[6] Understanding the risk factors associated with the development of ACS is paramount for timely diagnosis and intervention, thereby mitigating the associated morbidity and mortality.[7,8] Recent research endeavours have focused on exploring the utility of serum biomarkers in aiding the diagnosis, prognostication, and monitoring of ACS.[9–11]

MATERIALS and METHODS

This prospective cross-sectional observational study was conducted over 18 months (January 2023 to May 2024) in the Dr. Ram ManoharLohia Institute of Medical Sciences. This study followed the ethical principles and guidelines outlined in the Declaration of Helsinki. Ethical approval for the research was obtained from the Institutional Ethics Committee (IEC) of the Institute, under IEC approval number 81/22, as per letter number RC/516/RMLIMS, dated 22/08/2022. Written informed consent was obtained from all participants before their inclusion in the study. The confidentiality and anonymity of the participants' data were strictly maintained throughout the study to ensure compliance with ethical standards.

Study Population

The study enrolled adult patients aged 18–60 years, of either sex, presenting to the emergency department with suspected ACS due to fractures of the leg within 3 hours of injury.

Study Design

In a prospective cross-sectional observational study, 58 participants were included, determined by sample size calculation based on the prevalence of ACS and required statistical power.

Sample Size Calculation

The required sample size was calculated based on the prevalence of ACS, desired statistical power, and expected differences in serum biomarkers. Using a 95% confidence level (z=1.96) and 80% power (z=0.84), the following formula was applied:

$$n = ((\sigma_1^2 + \sigma_2^2)/k) \times (z_{1-\alpha/2} + z_{1-\beta})^2 / \Delta^2$$

Where:

- n = sample size
- σ^2 = variance
- Δ = difference in means
- k = ratio of group sizes (assumed 1)
- $z_{1-\alpha/2} = 1.96$ (for 95% CI)
- $z_{1-\beta} = 0.84$ (for 80% power)

Mean bicarbonate levels were 23.3 mmol/L for the ACS group and 26.6 mmol/L for the fracture group, giving a mean difference (Δ) of -3.3 mmol/L. The variances were 37.21 and 33.64, respectively. Based on these inputs, the required sample size was 52 per group. Including a 10% attrition rate, the adjusted sample size was 58, which was rounded to 60 per group to ensure data reliability.

Data Collection

Data collection involved a comprehensive evaluation of patients presenting with suspected ACS secondary to leg fractures. Following informed consent, each patient underwent a detailed clinical assessment emphasizing the classical "5 P's" of compartment syndrome—Pain, Pallor, Pulselessness, Paraesthesia, and Paralysis. In addition, demographic and clinical data such as age, sex, occupation, personal habits, and fracture characteristics were systematically documented. Fracture type and location were confirmed through radiographic imaging, including anteroposterior (AP) and lateral views of the leg, knee, and ankle. Blood samples were collected at the time of admission from all patients for biochemical analysis, includ-

ing serum CK, potassium, lactate, bicarbonate, and chloride levels, to ensure standardization and eliminate methodological concerns. Creatine kinase levels were analyzed using the DGKC method, while lactate levels were determined through arterial blood gas (ABG) analysis. Intercompartmental pressure was measured using Whiteside's technique, a reliable and cost-effective method for indirectly assessing intracompartmental pressure. Introduced by L.A. Whiteside in 1975, this technique utilizes a simple manometric setup. A needle is inserted into the affected muscle compartment and connected via tubing to a mercury manometer or similar device, with a saline column indicating the pressure level. This method is especially advantageous in emergency and resource-constrained settings due to its simplicity and accuracy.[12]

An intracompartmental pressure threshold of 30 mmHg is widely recognized in clinical practice as indicative of significantly elevated pressure. Pressures at or above this level may compromise capillary perfusion, potentially resulting in ischemia and irreversible tissue damage if not promptly managed. Consequently, surgical intervention in the form of fasciotomy may be considered when this threshold is met, particularly in the presence of compatible clinical signs. Moreover, a differential pressure (ΔP)—calculated as the diastolic blood pressure minus the intracompartmental pressure—of less than 30 mmHg is also used as a critical indicator for surgical decompression. Patients in the study were stratified based on this 30 mmHg threshold to distinguish those with clinically significant pressure elevations from those with normal or borderline levels. This classification facilitated meaningful comparisons of clinical outcomes and correlations between pressure measurements and systemic indicators of tissue viability.[13,14]

Inclusion Criteria

1. **Age range:** Patients aged between 18 to 60 years were considered eligible, as this age group typically represents the most active demographic and reduces age-related physiological variability.
2. **Sex:** Both male and female patients were included to allow for gender-based comparison and ensure the generalizability of the findings.
3. **Clinical presentation:** Only patients presenting with clinical signs and symptoms suggestive of raised intracompartmental pressure (e.g., severe pain disproportionate to the injury, pain on passive stretch, paraesthesia, pallor, and tense swelling) following acute leg fractures (including tibial or fibular fractures) were included.
4. **Time of presentation:** Patients who reported to the hospital or trauma centre within three hours of sustaining the injury were included to ensure early-phase compartment changes were captured and to minimize confounding due to delayed presentation.
5. **Consent:** The study included only patients (or their legally authorized representatives) who provided written informed consent.

Exclusion Criteria

1. **Age restriction:** Patients younger than 18 years or older than 60 years were excluded to avoid age-related metabolic or vascular differences that could affect compartmental physiology.
2. **History of prior limb trauma:** Individuals with a history of previous fractures, surgeries, or soft tissue injuries in the affected limb were excluded, as such history could alter baseline tissue characteristics and confound the intracompartmental pressure readings.
3. **Comorbid medical conditions:** Patients with known comorbidities, such as diabetes mellitus, chronic kidney disease, or peripheral vascular disease, were excluded to eliminate confounding factors related to impaired wound healing, altered pain perception, or vascular compromise.
4. **Life-threatening injuries:** Polytrauma patients or those presenting with life-threatening conditions requiring immediate resuscitation or surgery were excluded, as the primary focus was isolated intracompartmental pressure assessment.
5. **Bleeding and coagulation disorders:** Patients with bleeding tendencies, including those on anticoagulant therapy or diagnosed with hemophilia or thrombocytopenia, were excluded to avoid complications in pressure measurement and outcomes.
6. **Vascular disorders:** Individuals with pre-existing varicose veins, deep vein thrombosis (DVT), or chronic venous insufficiency were excluded, as these conditions may alter intracompartmental pressures independently of trauma.
7. **Non-compliance or inability to consent:** Patients who were non-cooperative, unconscious, or unable to provide informed consent, and for whom no legal representative was available, were also excluded.

Statistical Analysis

Data collected from the study were entered into Microsoft Excel and analyzed using SPSS version 24.0 (IBM Corp., Armonk, NY, USA). Data were initially entered and cleaned in

Table 1. Descriptive statistics of intracompartmental pressure among the study participants (n=60)

	Mean	SD	Median	Percentiles		Range
				25th	75th	
Intracompartmental pressure	27.57	9.434	26.5	20	35.75	35

SD: Standard deviation

Table 2. Descriptive statistics of age of the study participants(n=60)

	Mean	SD	Median	Percentiles		Range
				25th	75th	
Age (years)	38.82	8.804	38	33.25	44.75	43

Microsoft Excel before being imported into SPSS. Descriptive statistics, including frequencies, percentages, means, medians, standard deviations, and interquartile ranges, were calculated to summarize the demographic, clinical, and biochemical data. The comparison of categorical variables between the two groups (intracompartmental pressure ≤30 mmHg vs. >30 mmHg) was performed using the chi-square test, while continuous variables were compared using the independent t-test. Pearson correlation was applied to assess the relationship between serum biomarkers (such as creatine kinase, lactate, potassium, etc.) and intracompartmental pressure. A multivariate regression analysis was conducted to determine the odds ratio for ACS development based on the biomarkers. Blood urea nitrogen (BUN) and potassium were excluded due to their strong correlation with renal function, which posed a risk of systemic confounding in the analysis. Lactate and creatine kinase were retained as they reflect distinct physiological processes (tissue hypoperfusion and muscle injury) and did not demonstrate multicollinearity with the other independent variables in preliminary analyses. Statistical significance was defined as a p-value < 0.05.

RESULTS

Demographic variables (age, gender, BMI) were statistically compared between groups, showing no significant differences, confirming homogeneity and reducing potential confounding in serum biomarker analysis. The results of the study demonstrate that the significant mean intracompartmental pressure was 27.57±9.43 mmHg. The median value was 26.5 mmHg, with the 25th and 75th percentiles at 20 and 35.75 mmHg, respectively. The range of intracompartmental pressure was 35 mmHg (Table 1). The mean age of the participants was 38.82±8.80 years. The median age was 38 years, with the 25th and 75th percentiles at 33.25 and 44.75 years, respectively. The age range was 43 years (Table 2).

BUN levels had a mean of 17.03±1.62 mg/dL, showing low variability and a range of 5.9 mg/dL. Bilirubin levels were similarly low, with a mean of 0.6533±0.13 mg/dL and a range of 0.52 mg/dL. Liver enzyme levels exhibited greater variability, with SGPT (alanine transaminase) having a mean of 76.78±15.60 U/L and a range of 44 U/L, while SGOT (aspartate transaminase) showed a mean of 45.96±14.20 U/L and a range of 41.5 U/L. Urea levels displayed the highest variability, with a mean of 41.97±13.53 mg/dL and a range of 65.1 mg/dL. Creatinine levels, prothrombin time (PT), and INR demonstrated lower variability, with means of 0.965±0.17 mg/dL, 13.57±2.09 seconds, and 1.003±0.08, respectively. These findings highlight that while markers like BUN, bilirubin, and creatinine are tightly clustered, others such as urea and liver enzymes (SGPT, SGOT) show more substantial variability (Table 3).

Among 60 study participants, 38 had intracompartmental pressure ≤30 mmHg, and 22 had intracompartmental pressure >30 mmHg. Pain and paralysis were observed in 100% of patients in both groups (n=60). Pallor was noted in 57.9% (n=22) of patients with intracompartmental pressure ≤30 mmHg, compared to 27.3% (n=6) of those with pressure >30 mmHg—a statistically significant difference (p=0.032). Pulselessness was present in 86.8% (n=33) of patients with intracompartmental pressure ≤30 mmHg, compared to 54.5% (n=12) of those with pressure >30 mmHg, also statistically significant (p = 0.011). Similarly, paraesthesia was observed in 86.8% (n=33) of patients with intracompartmental pressure ≤30 mmHg but only in 54.5% (n=12) of those with pressure >30 mmHg (p=0.011) (Table 4 and Fig. 1).

Table 3. Descriptive statistics of Biochemical Markers among the study participants (n=60)

Variables	Mean	SD	Median	Percentiles		Range
				25th	75th	
BUN	17.03	1.6174	17.3	15.8	18.375	5.9
Bilirubin	0.6533	0.12577	0.66	0.56	0.7575	0.52
SGPT	76.783	10.7042	78	68	84	44
SGOT	45.965	10.0897	45	39	54.5	41.5
Urea	41.972	17.0328	37.4	31.3	48.8	65.1
Creatinine	0.9653	0.28713	0.9	0.715	1.2	1.04
PT	13.567	0.4554	13.6	13.225	13.9	1.7
INR	1.0033	0.07512	0.99	0.94	1.06	0.28

BUN: Blood urea nitrogen; SGPT: Alanine transaminase; SGOT: Aspartate transaminase; PT: Prothrombin time; INR: international normalized ratio

Table 4. Association of acute compartment syndrome with clinical manifestations (n=60)

Variables	Suspected ACS patients (intracompartmental pressure in mmHg)				Total		p
	<=30 mmHg (n=38)		>30 mmHg (n=22)				
	n	%	n	%	n	%	
Pain	38	100.0	22	100.0	60	100.0	NA
Pallor	22	57.9	6	27.3	28	46.7	**0.032**
Pulselessness	33	86.8	12	54.5	45	75.0	**0.011**
Paraesthesia	33	86.8	12	54.5	45	75.0	**0.011**
Paralysis	38	100.0	22	100.0	60	100.0	NA

60 study participants, 38 patients had intracompartmental pressure ≤30mmHg whereas 22 had intracompartmental pressure>30 mmHg. ACS: Acute compartment syndrome

Creatine kinase levels were notably higher in patients with intracompartmental pressure >30 mmHg [median=1549.5 U/L, IQR=2700 (410.3–3110.5), mean=2117.02±1863.37] compared to those with pressure ≤30 mmHg [median =665.5 U/L, IQR=847.8 (338.8–1186.5), mean=1117.18±1493.39], with a statistically significant difference (p=0.019). Lactate levels were also significantly elevated in the >30 mmHg group (mean=2.39±0.56 mmol/L) compared to the ≤30 mmHg group (mean =1.99±0.78 mmol/L, p=0.033). Potassium levels were higher in the ≤30 mmHg group (mean=4.47±0.54 mmol/L) compared to the >30 mmHg group (mean=4.06±0.47 mmol/L, p=0.005). BUN levels were significantly higher in the >30 mmHg group (mean=18.14±0.98 mg/dL) compared to the ≤30 mmHg group (mean=16.39±1.57 mg/dL, p=0.0001). Other biochemical markers, including bicarbonate, chloride, D-dimer, HbA1c, RBS, bilirubin, SGPT, SGOT, urea, creatinine, PT, and INR, did not show significant differences between the groups (Table 5 and Fig. 2, 3).

Creatine kinase and lactate levels were significantly higher in the >30 mmHg group, indicating greater muscle damage and tissue hypoxia, respectively. Potassium levels were elevated in the ≤30 mmHg group, potentially reflecting cellular injury. BUN levels were also significantly higher in the >30 mmHg group, suggesting compromised renal function in severe cases (Table 6, Fig. 4).

A binomial multivariate logistic regression analysis was conducted to evaluate the impact of biochemical markers on the likelihood of developing ACS. The Hosmer-Lemeshow test confirmed the model's fit (χ^2 = 3.050, p = 0.931). The model explained 65.9% of the variance in ACS development (Nagelkerke R^2). Creatine kinase and lactate were the only significant predictors. Patients with creatine kinase

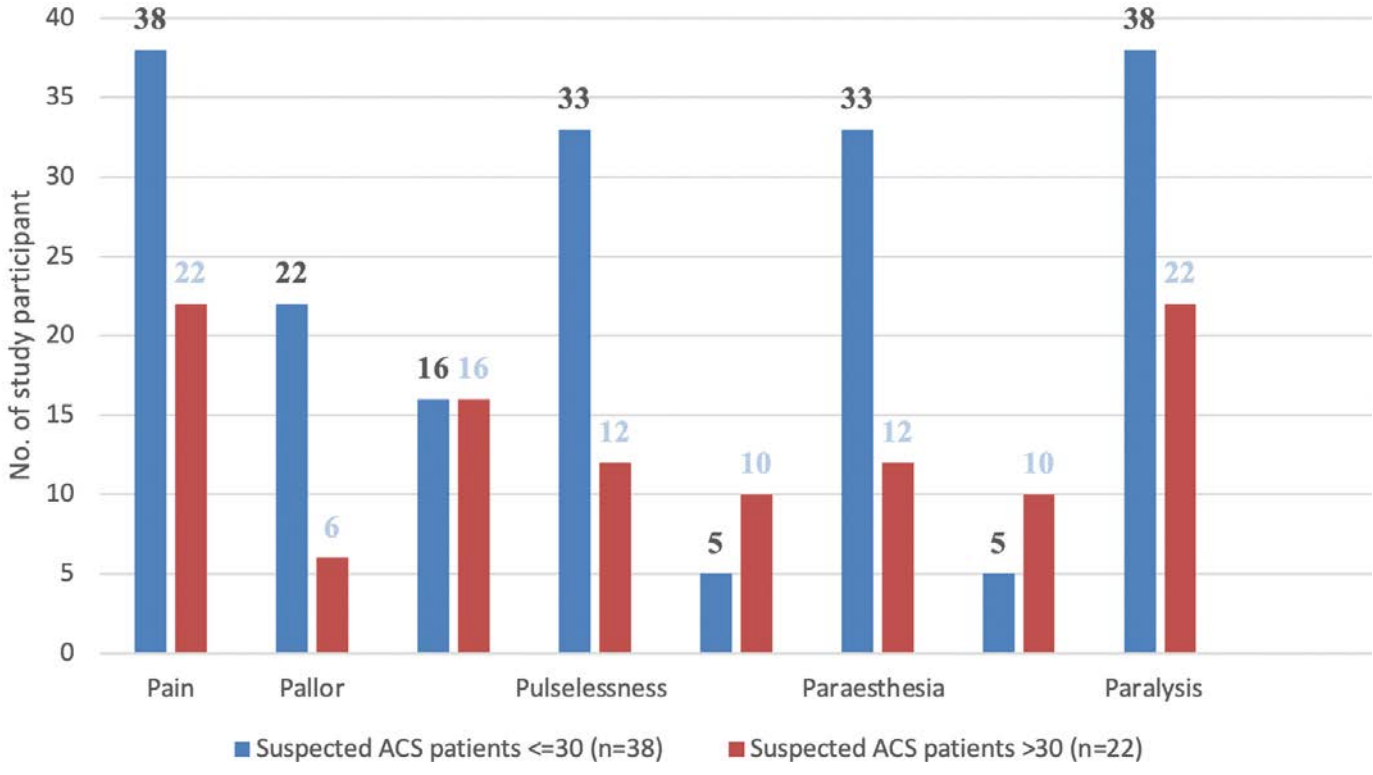

Figure 1. Association of Acute Compartment syndrome with clinical manifestations

ACS: Acute compartment syndrome

levels of 3000–6000 U/L had 2.5 times higher odds, and those with levels of 1000–3000 U/L had 1.11 times higher odds of developing ACS compared to those with levels <500 U/L. Similarly, patients with lactate levels ≥2 mmol/L had 1.5 times higher odds of developing ACS than those with levels <2 mmol/L (Table 7).

DISCUSSION

This study assessed the correlation of serum biomarkers with intracompartmental pressure monitoring in diagnosing ACS in the leg. The primary objective of the study was to measure the serum biomarkers in suspected cases of acute compartment syndrome. ACS was suspected in patients with intracompartmental pressure above or equal to 30 mmHg.

The mean intracompartmental pressure among the study participants was 27.57±9.434 mmHg. Of the 50 patients, 22 (44%) had intracompartmental pressures exceeding 30 mmHg. Comparable findings were reported by Valdez et al.,[15] who studied 97 patients with isolated tibia or fibula fractures or extremity compartment syndrome (CS), identifying CS in 39 patients (40%). Similarly, Weingart et al.[4] analyzed 930 patients meeting inclusion criteria, of whom 389 (41.8%) presented to the emergency department with acute compartment syndrome, and 541 (58.2%) presented with tibia or fibula fractures. Nilsson et al.[16] reported intercompartmental pressure (compartment with the highest pressure) was lower in patients with fractures (median 45 mmHg, range 25–90 mmHg) compared with those without fractures (median 83 mmHg, range 18–130 mmHg), p<0.05.

We found the median CK value in patients with suspected ACS to be 665.5 [IQR=847.8] in those with intracompartmental pressure ≤30 and 1549.5 [IQR=2700] in those with intracompartmental pressure >30. This difference was statistically significant (p-value=0.019). In our study, CK between 3000–6000 U/L had 2.5 times higher odds than those <500 U/L of having ACS.

In a study by Weingart et al.,[4] the odds of having ACS increased with increasing CK values. Of the 41 patients with a CK >5000 U/L, 29 (70.7%) had ACS, and 12 (29.3%) had a tibia/fibula fracture. The mean CK levels were 2132.8 U/L (SD=7265.3), and on comparing them to those with tibial fracture and without compartment syndrome, the difference was statistically significant (p<0.01).

Table 5. Comparison of mean values of biochemical markers based on Acute Compartment Syndrome (n=60)

Variables	Suspected ACS patients (intracompartmental pressure in mmHg)		t value	95% Confidence interval		p*
	<=30 mmHg (n=38)	>30 mmHg (n=22)		Lower	Upper	
Creatine kinase [median (IQR)]	665.5 (847.8)	1549.5 (2700)	–	–	–	0.019#
Bicarbonate	22.37±1.74	23.44±2.63	-1.887	-2.199	0.064	0.64
Chloride	117.84±14.30	115.41±11.86	0.674	-4.79	9.65	0.503
Lactate	1.99±0.78	2.39±0.56	-0.2184	-0.776	-0.033	0.033
Potassium	4.47±0.54	4.06±0.47	2.962	0.126	0.676	0.005
BUN	16.39±1.57	18.14±0.98	-4.696	-2.49	-1.00	0.0001
D-dimer	0.60±0.12	0.57±0.12	1.060	-0.030	0.100	0.293
HbA1c	5.75±0.87	5.85±0.66	-0.433	-0.521	0.336	0.667
RBS	169.08±73.01	152.95±45.47	0.934	-18.41	50.66	0.354
Bilirubin	0.65±0.12	0.66±0.13	-0.374	-0.080	0.055	0.710
SGPT	76.21±10.10	77.77±11.86	-0.541	-7.33	4.21	0.590
SGOT	45.42±9.53	46.91±11.16	-0.546	-6.92	3.95	0.587
Urea	43.71±18.35	38.97±14.39	1.040	-4.38	13.87	0.303
Creatinine	0.99±0.29	0.92±0.28	0.958	-0.080	0.227	0.342
PT	13.56±0.43	13.57±0.51	-0.078	-0.255	0.236	0.938
INR	1.01±0.08	1.00±0.07	0.224	-0.036	0.045	0.824

*: Significant differences mean values of creatine kinase (p=0.019), lactate (p=0.033), potassium (p=0.005) and BUN (p=0.0001). ACS: Acute compartment syndrome; IQR: Interquartile range; BUN: Blood urea nitrogen; HbA1c: Hemoglobin A1c; RBS: Random blood sugar; SGPT: Alanine transaminase; SGOT: Aspartate transaminase; PT: Prothrombin time; INR: International normalized ratio

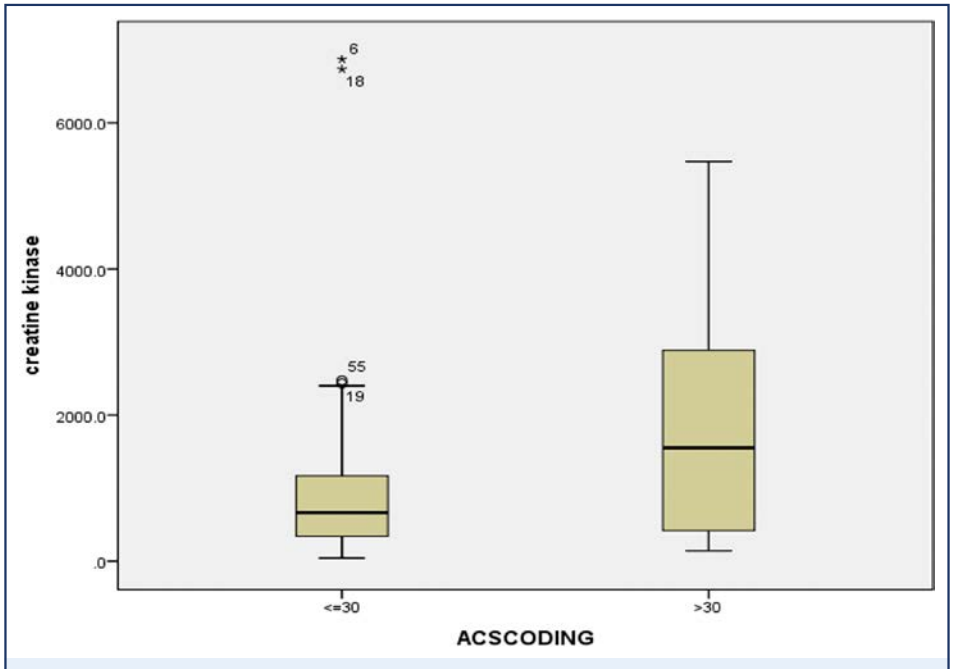

Figure 2. Creatine kinase according

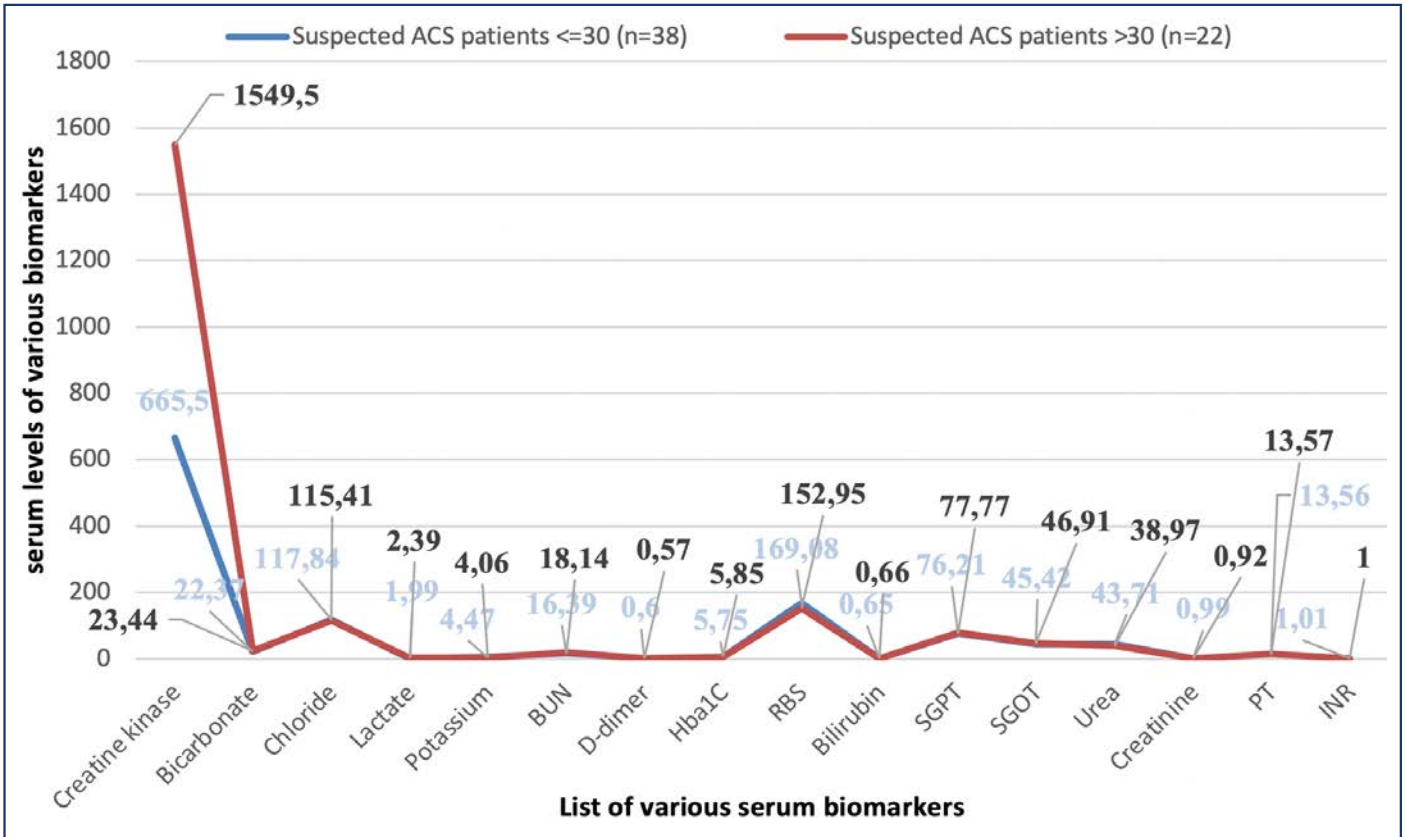

Figure 3. Comparison of mean values of biochemical markers based on Acute

In another study by Valdez et al.,[15] the mean creatine kinase (CK) (minimum values during the hospital stay) in those with compartment syndrome was 1824.1 (SD=3174.8), and the maximum mean CK values were as high as 55,710.9 (SD=106,887.4). On comparing these values to those with tibial fractures but without compartment syndrome, the difference in CK levels was statistically significant (p<0.0001). The suggestion that elevated levels of CK are linked to compartment syndrome (CS) appears reasonable.

In our study, the mean serum lactate levels were 1.99±0.78 in patients with intracompartmental pressure ≤30 mmHg and 2.39±0.56 in those with pressure >30 mmHg, with a statistically significant difference (p=0.033). Valdez et al.[15] reported higher serum lactate levels in tibial fracture patients with compartment syndrome (mean 8.6±7.0 vs. 3.7±2.4, p=0.0015).[12] Weingart et al.[4] found a mean lactate of 2.7±4.12 in ACS patients compared to 2.3±2.29 in fracture patients. Higher lactate levels correlate with increased ACS risk, with lactate >5 mmol/L showing 2.4 times higher odds of ACS.

Another biomarker that is significantly different based on intracompartmental pressure less than or more than 30 was serum potassium (p=0.033). In those with intracompartmental pressure ≤30, the mean serum potassium levels were 4.47±0.54, and in those >30, it was 4.06±0.47.

In the study by Valdez et al.,[15] the mean potassium was also statistically significant (p=0.0036). Weingart et al.[4] reported a significant difference (p<0.01) in serum potassium levels across both studied groups in their study (4.1 [SD=0.6] vs. 4.0 [SD=0.5]).

We also found that mean BUN levels were significant across both groups (p=0.001). In another study, the mean BUN was 17.3 (SD=14.8) in the ACS group, whereas in the group with no ACS, the BUN was 15.0 (SD=10.2). This difference in their study was also statistically significant (p=0.03). They also reported that BUN more than 50 mg/dL had 2.38 times higher odds of predicting ACS.[15]

The difference in serum bicarbonate was not statistically significant across both groups (p=0.64). Serum bicarbonate did not show a significant association with the diagnosis of ACS in our study. This may be explained by the fact that many patients presented during the early stages (within three hours of sustaining the injury) of compartment syn-

Table 6. Association of acute compartment syndrome with serum biomarkers (n=60)

Serum biomarkers	Suspected ACS patient (intracompartmental pressure in mmHg)				p
	≤30 mmHg (n=38)		>30 mmHg (n=22)		
	n	%	n	%	
Creatine Kinase					
Normal (<500 U/L)	14	38.9	6	27.3	**0.005**
Abnormal (≥500 U/L)	24	61.1	16	72.7	
Bicarbonate					
Normal (>20mEq/L)	32	84.2	19	86.4	1.000
Abnormal (10-20 mEq/L)	6	15.8	3	13.6	
Chloride					
Normal (100–150 mEq/L)	34	89.5	19	86.4	1.000
Abnormal (<100 mEq/L)	4	10.5	3	13.6	
Lactate					
Normal (1–2 mmol/L)	23	62.2	4	18.2	**0.001**
Abnormal (>2 mmol/L)	14	37.8	18	81.8	
Potassium					
Normal (3–5 mEq/L)	31	81.6	22	100.0	**0.040**
Abnormal (>5mEq/L)	7	18.4	0	0.0	
Urea					
Normal (<40 mg/dL)	20	52.6	15	68.2	0.426
Abnormal (≥40 mg/dL)	18	47.4	7	31.8	
Creatinine					
Normal (<1 mg/dL)	23	60.5	12	54.5	0.787
Abnormal (≥1 mg/dL)	15	39.5	10	45.5	

Significant p-value in Creatine kinase =0.005, Lactate=0.001*, Potassium=040*. ACS: Acute compartment syndrome

Table 7. Binary Logistic regression analysis for association of biochemical parameters with acute compartment syndrome (n=60)

Parameters	Adjusted OR	p	95% CI	
			Lower	Upper
Creatine Kinase				
3000–6000	2.500	0.025	1.403	15.501
1000–3000	1.111	0.029	1.48	8.367
500–1000	0.833	0.858	0.114	6.111
<500	Reference			
Bicarbonate				
10–20	1.187	0.822	0.266	5.310
>20	Reference			
Chloride				
<100	0.745	0.718	0.151	3.686
100–150	Reference			
Lactate				
>=2	1.541	0.039	1.33	2.203
<2	Reference			
Urea				
<40	0.599	0.183	0.282	1.273
>=40	Reference			
Creatinine				
<1	1.278	0.651	0.442	3.695
1–1.5	Reference			

OR: Odds ratio; CI: Confidence interval

drome, before significant systemic metabolic acidosis could develop. Biomarkers like lactate and creatine kinase, which more directly reflect localized muscle ischemia and cellular injury, likely provided stronger diagnostic value, reducing the apparent contribution of bicarbonate in our statistical model. Unlike our study, this difference was statistically significant (p<0.001) in one study, which also reported that bicarbonate levels between 10–20 mmol/L had 2.41 higher odds of predicting ACS.[15]

There were certain limitations in the study. Patients were evaluated only once, i.e., at the time of admission. They were not followed up for the biomarker levels during their hospital stay or before or after any intervention was done. So, further studies should be done to evaluate the trend of these biomarkers, especially CK, lactate, potassium, BUN, and bicarbonate, during the duration of stay and before and after any surgical intervention done for compartment syndrome. This study did not have any control group, which could have been a better design to study the outcome of biomarkers in patients with and without compartment syndrome. Thirdly, a small sample size makes it difficult to generalize the results on a community level. So, studies of larger sample sizes should be done to make the results more generalized, representing a larger population. The potential influence of fasting status and medication use on serum biomarker levels was not standardized in this study due to the emergent nature of patient presentation, which may have introduced variability in the results.

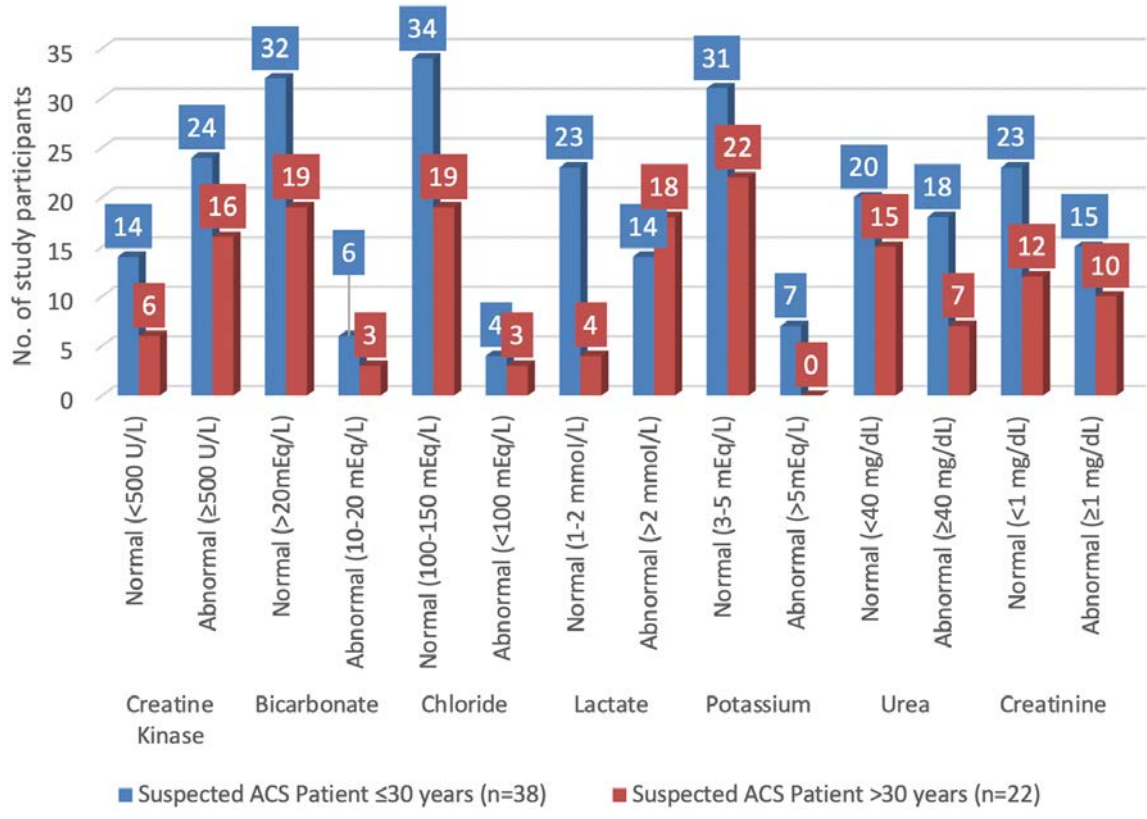

Figure 4. Association of Acute Compartment Syndrome with serum biomarkers (n=60)

ACS: Acute compartment syndrome

CONCLUSION

Our study shows that serum biomarkers, especially CK, lactate, BUN, and potassium, have a significant association with elevated intracompartmental pressure, supporting the potential role of these markers in diagnosing ACS in leg fractures. The relationship of increased CK, lactate (>2 mmol/L), and BUN, along with potassium changes, with increased intracompartmental pressure forms the basis for diagnosing ACS. These findings further emphasize the importance of serum biomarkers as a complement to intracompartmental pressure monitoring as a non-invasive tool for early ACS diagnosis and management. A larger sample size and longitudinal data studies will be needed to validate these biomarkers as reliable diagnostic tools. This study also underscores the medico-legal importance of serum biomarkers in diagnosing ACS because elevated CK and lactate levels and clinical findings provide crucial evidence for timely intervention. The correct identification of ACS may prevent legal repercussions from delayed treatment and patient harm.

Disclosures

Ethics Committee Approval: The study was approved by the Dr. Ram ManoharLohia Institute of Medical Sciences Ethics Committee (No: 81/22, Date: 22/08/2022).

Informed Consent: Informed consent was obtained from all participants.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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REFERENCES

1. Via AG, Oliva F, Spoliti M, Maffulli N. Acute compartment syndrome. Muscles Ligaments Tendons J 2015;5:18–22.
2. McQueen MM, Duckworth AD, Aitken SA, Court-Brown CM. Predictors of compartment syndrome after tibial fracture. J Orthop Trauma 2015;29:451–5. [CrossRef]
3. Singh AK, Tripathi SK, Singh RR, Yadav PK, Singh M, Verma AK. Evaluation of the effectiveness of road safety measures and their impact on the pattern and distribution of extracranial and intracranial hemorrhages in fatal head injury cases in Uttar Pradesh, India. Natl J Maxillofac Surg 2024;15494–8. [CrossRef]
4. Weingart GS, Jordan P, Yee KL, Green L. Utility of laboratory markers in evaluating for acute compartment syndrome in the emergency department. J Am Coll Emerg Physicians Open 2021;2:e12334. [CrossRef]
5. Schmidt AH. Acute compartment syndrome. Injury 2017;48(Suppl 1):S22–5. [CrossRef]
6. Whitesides TE, Heckman MM. Acute Compartment Syndrome: Update on diagnosis and treatment. J Am AcadOrthop Surg 1996;4:209–18. [CrossRef]
7. Shadgan B, Menon M, Sanders D, Berry G, Martin C. Current thinking about acute compartment syndrome of the lower extremity. Can J Surg 2010;53:329–34.
8. Rorabeck CH. The treatment of compartment syndromes of the leg. J Bone Joint Surg Br 1984;66:93–7. [CrossRef]
9. Shadgan B, Menon M, O'Brien PJ, Reid WD. Diagnostic techniques in acute compartment syndrome of the leg. J Orthop Trauma 2008;22:581–7. [CrossRef]
10. Smith JW, Chakravarthy V, Shafritz AB, Anderson ML. Biomarkers in acute lower-extremity compartment syndrome. Orthopedics. 2020;43:e17–25.
11. Lee C, Lin J, Lin C. The diagnostic role of serum levels of interleukin-6 in acute compartment syndrome after tibial fracture. Injury 2022;53(1):157–61.
12. Whiteside LA, Haney T, Morimoto K, White SE. Tissue pressure measurements as a determinant for the need of fasciotomy. Clin Orthop Relat Res 1975:43–51. [CrossRef]
13. Mubarak SJ, Hargens AR. Acute compartment syndromes. Surg Clin North Am 1981;61:1197–211.
14. McQueen MM, Court-Brown CM. Compartment monitoring in tibial fractures: The pressure threshold for decompression. J Bone Joint Surg Br 1996;78:99–104. [CrossRef]
15. Valdez C, Schroeder E, Amdur R, Pascual J, Sarani B. Serum creatine kinase levels are associated with extremity compartment syndrome. J Trauma Acute Care Surg 2013;74:441–5; discussion 445–7. [CrossRef]
16. Nilsson A, Alkner B, Wetterlöv P, Wetterstad S, Palm L, Schilcher J. Low compartment pressure and myoglobin levels in tibial fractures with suspected acute compartment syndrome. BMC Musculoskelet Disord 2019;20:15. [CrossRef]