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Serum albumin nadir as marker of inflammatory response in abdominal trauma

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Background: Serum albumin levels decrease following major trauma, for various reasons. We postulated that the serum albumin nadir (SAN) level would correlate negatively with severity of physiological insult.
Methodology: This retrospective cohort study included all patients with abdominal trauma admitted to the Trauma Intensive Care Unit at Inkosi Albert Luthuli Central Hospital during 2017 and 2018.
Results: Of the 87 patients, 70 (80.5%) were male. Mean age was 32.48 years (SD 11.65; range 12–73). Blunt trauma comprised 54 patients (62.1%). Median SAN level was 23 g/L (IQR 20–27; range 10–38). Median SAN level was not different between patients with blunt versus penetrating trauma ($p = 0.69$), patients in whom inotropic support had been used/not used ($p = 0.0502$), and no different between patients on the various modes of feeding at the time of SAN ($p = 0.14$). However, median SAN level was lower for patients with hollow visceral injury ($p = 0.004$), for patients who had undergone laparotomy ($p = 0.0006$), for those who had received damage control surgery ($p = 0.001$), those who had received blood transfusions ($p = 0.03$), and patients who died compared to survivors ($p = 0.02$). Univariate regression analysis revealed negative coefficients for the following in relation to SAN level: blood transfusion (-2.77; $p = 0.023$), hollow viscus injury (-3.21; $p = 0.008$), laparotomy (-4.5; $p < 0.001$), damage control surgery (-3.60; $p = 0.02$), day of SAN (-0.39; $p = 0.001$), ICU length of stay (-0.12; $p = 0.002$), and death (-3.27; $p = 0.03$).
Conclusion: Greater physiological insults lead to lower levels of SAN. Serum albumin nadir level may therefore have value as a prognostic indicator in the acute trauma setting.
Keywords: albumin, nadir, marker, trauma, inflammation

Introduction

Abdominal injuries pose a significant challenge due to their potential for severe complications.[1] Activation of the inflammatory cascade, while essential for the healing process, can also exaggerate tissue damage, leading to systemic complications.[2,3] Being able to monitor the magnitude of the inflammatory response may offer clinicians the ability to respond to the threat of complications more timeously.[4,5]

Serum albumin, most commonly known for its role in maintaining osmotic pressure and transporting various molecules, is increasingly being recognised for its potential as a diagnostic and prognostic marker in the aftermath of abdominal trauma.[4-6] The initial response post-trauma involves the activation of innate immune cells, such as neutrophils and macrophages, which trigger the release of pro-inflammatory cytokines.[7] These cytokines are responsible for the local inflammatory response that clears debris and initiates tissue repair.[7,8]

An excessive or prolonged inflammatory response can lead to increased tissue damage, severe organ dysfunction, and an increased risk of complications such as sepsis and multiple organ failure.[8] It is in this fine balance of processes that serum albumin emerges as a potential sentry of the body's response to the insult of trauma.[9-11]

Reduced serum albumin levels are observed in trauma patients for various reasons. Severe trauma can result in capillary leak syndrome, leading to the leakage of plasma proteins, including albumin, into the interstitial space. In the face of hypovolaemia, the body attempts to retain fluid, leading to dilutional hypoalbuminemia, tissue hypoperfusion and ischaemia, which can impair hepatic synthesis of albumin. Furthermore, during activation of the inflammatory cascade, certain cytokines suppress the synthesis of albumin. And in cases of abdominal trauma involving organ damage or rupture, albumin can be lost through the gastrointestinal tract, leading to decreased serum levels.[6,12-13]

The measurement of serum albumin levels may assist clinicians with a non-invasive method to assess the inflammatory response in patients who were involved in a trauma incident.[12-14] Lower albumin levels on admission have been associated with an increased incidence of complications including sepsis, wound infections, and prolonged hospital stay.[15] The monitoring of albumin levels over time can possibly assist treating physicians in identifying patients at risk of developing systemic complications, and

therefore grant the opportunity to respond with a timeous intervention.[6,12-14]

Factors such as pre-existing medical conditions, malnutrition, and hepatic dysfunction can influence albumin levels, potentially confounding our interpretation of its level in a trauma patient.[15,16] Usually, in the post-traumatic period, the serum albumin level decreases until it reaches a nadir, after which it gradually increases back to normal over days to weeks. The serum albumin nadir (SAN) level may be an indicator of the time when the traumatic insult and the ensuing inflammatory response have reached their maximum impact. Daily fluctuations in serum albumin values, on the other hand, are less helpful as they can be influenced by various factors. We postulated that the SAN level would correlate negatively with severity of physiological insult.

Methodology

A retrospective cohort study was conducted in the Trauma Intensive Care Unit, Inkosi Albert Luthuli Central Hospital (IALCH), Durban, South Africa. Patients included in the study were between 12 and 75 years of age, having sustained any form of abdominal trauma, and who survived for longer than four days from time of admission to the unit. Patients who were admitted to the unit more than five days from sustaining the injury were excluded. Data were collected by interrogation of a prospectively maintained electronic database.

Results

During the period under review (January 2017 to December 2018 inclusive) there were 563 admissions to the Trauma Intensive Care Unit, of which 87 patients met the inclusion criteria.

Demographics

Of the 87 patients, 70 (80.5%) were male. Mean age was 32.48 years (SD 11.65; range 12–73). Blunt trauma comprised 54 patients (62.1%), among which 27 (50%) were from motor vehicle collisions (MVC), 15 (28%) from pedestrian vehicle collisions (PVC), and 8 (15%) from assaults. Of the 33 patients (37.9%) with penetrating trauma, 24 (73%) had gunshot wounds (GSW) and 9 (27%) had stabs.

Injury severity and physiological insult

Median injury severity score (ISS) was 33 (IQR 22–45; range 9–64). Hollow visceral injury was present in 43 patients (49.4%). Blood transfusion was administered to 42 patients (48.3%), inotropic support was used in 32 patients (36.8%), laparotomy was performed on 58 patients (66.7%), and damage control surgery was employed in 17 patients (19.5%). Median ICU length of stay was 13 days (IQR 8–25; range 3–102). Of this cohort, 18 patients died, for a mortality of 20.7%.

Albumin nadir

SAN was reached at a median of 4 days after injury (IQR 2–7; range 1–28; Figure 1). Median SAN level was 23 g/L (IQR 20–27; range 10-38). Feeding at time of SAN was oral in 11 patients (12.6%), enteral in 44 patients (50.6%), parenteral in 1 patient (1.1%), and nil in 31 patients (35.6%).

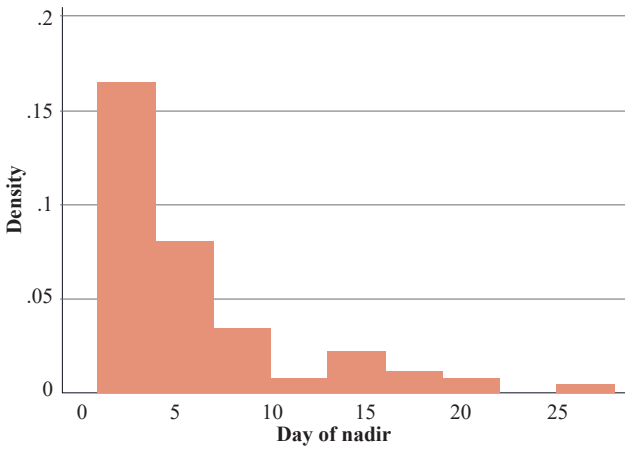

Figure 1: Histogram depicting day on which serum albumin nadir was reached

Day of SAN

The day on which SAN was reached did not differ significantly between the following groups: blunt vs penetrating mechanism (p = 0.56), hollow viscus injury (p = 0.14) blood transfusion vs none (p = 0.31), inotropes vs none (p = 0.42), laparotomy vs none (p = 0.79), damage control vs none (p = 0.17), and death (p = 0.11). There was however a significant difference in the day on which SAN was reached between the various modes of feeding (EN/PN [median 6] vs oral [median 4] vs nil [median 2]; p = 0.001). Spearman correlation was weakly positive for age vs day

Table I: Serum albumin level at time of nadir

	Nadir albumin (g/L)				
	n	Median	Q1	Q3	*p*-value
Mechanism of injury					
Blunt	54	24.0	20.0	27.0	0.69
Penetrating	33	22.0	19.0	28.0	
Hollow viscus injury					
Absent	44	25.5	22.0	28.0	**0.004**
Present	43	22.0	19.0	24.0	
Blood transfusion					
No	45	24.0	22.0	29.0	**0.03**
Yes	42	22.0	19.0	27.0	
Received inotropes					
No	55	24.0	20.0	28.0	0.0502
Yes	32	22.0	19.0	25.0	
Laparotomy					
No	29	26.0	24.0	30.0	**0.0006**
Yes	58	22.0	19.0	25.0	
Damage control surgery					
No	70	24.0	20.0	28.0	**0.001**
Yes	17	21.0	19.0	22.0	
Feeds at time of nadir albumin					
EN / PN	45	24.0	20.0	27.0	0.14
Oral	11	27.0	23.0	29.0	
Nil	31	22.0	19.0	26.0	
Outcome					
Discharge	69	24.0	21.0	28.0	**0.02**
Death	18	20.0	16.0	24.0	

Table II: Univariate regression – serum albumin level at time of nadir

	Nadir albumin (g/L)		
	Coefficient	**SEM**	***p*-value**
Age (years)	-0.08	0.05	0.13
Penetrating trauma	-0.53	1.27	0.68
ISS	0.03	0.04	0.47
Hollow viscus injury present	-3.21	1.19	**0.008**
Received blood transfusion	-2.77	1.20	**0.023**
Received inotropes	-2.44	1.25	0.055
Underwent laparotomy	-4.50	1.22	**< 0.001**
Underwent damage control surgery	-3.60	1.51	**0.02**
Day of nadir albumin	-0.39	0.11	**0.001**
No feeds at time of nadir albumin	-	-	-
EN / PN feeds at time of nadir albumin	1.42	1.33	0.29
Oral feeds at time of nadir albumin	3.62	2.00	0.07
Length of ICU stay (days)	-0.12	0.04	**0.002**
Death	-3.27	1.48	**0.03**

SAN was reached (0.22; $p = 0.04$) and moderately positive for length of ICU stay vs day SAN was reached (0.37; $p = 0.0004$).

SAN level

Median SAN level was no different between patients with blunt versus penetrating trauma ($p = 0.69$), no different between patients who had and had not received inotropic support ($p = 0.0502$), and there was also no difference in median SAN level between the various modes of feeding at the time of SAN ($p = 0.14$). However, median SAN was lower for patients with hollow visceral injury than those without ($p = 0.004$), lower for patients who had undergone laparotomy ($p = 0.0006$), lower for those who had received damage control surgery ($p = 0.001$), lower for those who had received blood transfusions than those who had not ($p = 0.03$), and lower for patients who died compared to survivors ($p = 0.02$) (Table I).

The Spearman correlation coefficient for SAN level vs ICU length of stay was -0.40 ($p = 0.002$) and for SAN level vs day of SAN it was -0.28 ($p = 0.009$). There was no significant correlation between SAN level and age or ISS.

Univariate regression analysis revealed negative coefficients for the following in relation to SAN level: blood transfusion (-2.77; $p = 0.023$), hollow viscus injury (-3.21; $p = 0.008$), laparotomy (-4.5; $p < 0.001$), damage control surgery (-3.60; $p = 0.02$), day of SAN (-0.39; $p = 0.001$), ICU length of stay (-0.12; $p = 0.002$), and death (-3.27; $p = 0.03$) (Table II).

Discussion

The provided results offer a comprehensive overview into various aspects of patient demographics, injury mechanisms, treatment approaches, and outcomes in a cohort of trauma patients in Southern Africa. This correlates with numerous studies done on trauma in this country.[17-19] This study highlights the relationship between SAN levels and the use thereof in various clinical situations. Monitoring serum albumin levels could provide clinicians with valuable information about the severity of trauma and the potential for adverse outcomes. It may also serve as an indicator of the effectiveness of interventions and treatment strategies. It is readily available and not expensive. The SAN might be used to stratify patients for ICU eligibility when bed shortage becomes a determining factor and might inform the clinician as to the patients who require more intensive care and vigilance. As far as we are aware, no other study in abdominal trauma has looked at SAN as a biomarker or a prognostic factor, but other studies in medicine have alluded to this as a marker of prognostication.[20-23]

This study had a significant male predominance (80.5%). The mean age of patients was 32.48 years, with a wide range of ages (12–73 years) indicating the diversity of patients within the cohort. These demographics correlate with other similar studies done in Southern Africa.[17-19] The majority of injuries were due to blunt trauma (62.1%), with MVC and PVC being the leading causes, followed by assaults. These results are similar to other studies done in Africa.[24] Penetrating trauma accounted for 37.9% of cases, with GSWs being the most common form. This study also highlighted the presence of hollow visceral injuries in almost half of the patients (49.4%). These findings appear to be unique to low- to middle-income countries (LMICs) as penetrating injuries in the first world are more commonly stabbings and accidental in nature, with the exception of the USA, but this also is changing. This might have an influence on albumin readings and responses of the inflammatory cascade to the different mechanisms of injuries.[25-27]

SAN was reached at a median of 4 days after injury in the current cohort. The median SAN level was 23 g/L. It is notable that there were different modes of feeding at the time of SAN, with oral, enteral, parenteral, and nil per mouth being the options. A significant difference was found in the day on which SAN was reached based on the mode of feeding, with patients on enteral or parenteral feeding reaching SAN later than those on oral feeding. The significance of this finding is unclear; although it is well known that feeding results in improved albumin levels and shorter hospitalisation.[27] It would be difficult to assume that nutrition would have a significant impact on the serum albumin level at such an early stage after major trauma.

Spearman correlation coefficients revealed weak positive correlations between age and the day SAN was reached, as well as a moderate positive correlation between ICU length of stay and the day SAN was reached. These findings correlate weakly with other studies done looking at SAN.[20,21] Interestingly, there was no significant correlation between SAN levels and age or ISS in our patient population.

Peterson et al. studied 414 patients hospitalised for heart failure and found that hypoalbuminemia assessed using the nadir level rather than the admission level, was associated with an increased risk of acute worsening of renal function – suggesting that the timing of serum albumin measurement may influence its utility as a biomarker.[20] Although we cannot extrapolate those findings to our patient population, we confirm that the nadir appears more valuable than albumin levels at other times.

Our findings shed some light on the relationship between SAN levels and patient outcomes. It appears that lower median SAN levels were associated with several factors,

including hollow visceral injury, undergoing laparotomy, receiving damage control surgery, receiving blood transfusions, and mortality. These associations suggest that lower SAN levels might be indicative of more severe injuries and worse patient outcomes. This is supported by the univariate analyses performed.

While this study provides some valuable insights into the relationship between SAN levels and patient outcomes, there are limitations that must be considered. The retrospective nature of this study and the relatively small sample size might limit the generalisability of the findings to the international stage or to bigger datasets. Using only patients requiring ICU admission means that concomitant injuries might increase the overall inflammatory response in these patients and influence the SAN levels. Our study design prevents the establishment of causal relationships between SAN levels and other clinical factors. However, further research with larger sample sizes and prospective designs is needed to validate these findings and explore the underlying mechanisms and usages of SAN.

Conclusion

This study offers valuable insights into the complex interplay between serum albumin levels, clinical variables and patient outcomes in trauma cases. The findings highlight the potential of SAN levels as a prognostic indicator in trauma patients.

Conflict of interest

The authors declare no conflict of interest.

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Ethical approval

Ethical requirements fulfilled. Approval from University of KwaZulu-Natal Biomedical Research Ethics Committee (BCA207/09).

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