Comparison Of S100b Levels In Saliva And Serum In Non-Operative Head Injury Patients At RSUP Ham (March – June 2023)

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ABSTRACT

Background: Traumatic brain injury (TBI) is a significant health concern, with mild to moderate cases comprising most occurrences. Early detection of intracranial hemorrhage is critical for preventing complications. While CT scans are widely used, many are unnecessary. S100B, a biomarker linked to blood-brain barrier disruption, has shown potential for TBI assessment. While serum S100B is well studied, its presence in saliva remains underexplored as a diagnostic tool.
Methods: This cross-sectional study analyzed S100B levels in serum and saliva of non-operative TBI patients at RSUP H. Adam Malik Medan from March to June 2023. Blood and saliva samples were collected and statistically analyzed, including ROC curve evaluation, to determine biomarker accuracy.
Results: Among 20 patients, serum S100B levels ranged from 0.69 to 62.05 µg/L (mean: 28.53 ± 3.06 µg/L), while salivary levels were higher, ranging from 13.4 to 63.98 µg/L (mean: 47.53 ± 2.85 µg/L). A strong correlation was observed between S100B levels and intracranial hemorrhage ($R^2 = 0.9966$), indicating saliva as a viable diagnostic medium.
Discussion: S100B plays a crucial role in TBI assessment. It helps predict intracranial hemorrhage and guides clinical decision-making. While serum S100B is widely accepted, salivary S100B offers a non-invasive alternative, making it a promising tool for early TBI detection. However, further studies with larger sample sizes are necessary to validate its clinical utility.
Conclusion: S100B is a reliable TBI biomarker, and its detection in saliva provides a non-invasive alternative to serum testing. This method could improve early diagnosis, reduce unnecessary CT scans, and enhance patient care.

Keywords: Traumatic brain injury, S100B, biomarker, intracranial hemorrhage, saliva testing, non-invasive diagnosis.

INTRODUCTION

Traumatic brain injury (TBI) is a frequent medical emergency, with over three million cases annually in the United States. According to the Scandinavian Neurotrauma Committee (SNC), mild to moderate TBIs account for 95% of all cases, predominantly caused by traffic accidents and falls. Intracranial hemorrhage, a common complication, significantly elevates mortality and disability risks. Although bleeding may occur at the time of impact, it often develops hours post-injury, leading to increased intracranial pressure, brain herniation, and death. Despite the widespread use of CT scans, studies indicate that only a small fraction of mild and moderate TBI patients exhibit detectable intracranial pathology.[1-3]

Mild TBI can induce axonal injury, neuroinflammation, and glial activation, all of which contribute to cognitive and sensory impairments. Additionally, it can disrupt the blood-brain barrier (BBB), increasing susceptibility to secondary hemorrhage. Early identification of BBB dysfunction is critical for predicting long-term disability. Several studies have explored serum biomarkers for early intracranial injury detection, with S100B emerging as one of the most reliable. S100B correlates with multiple BBB integrity indices and has demonstrated a 99% negative predictive value for ruling out intracranial hemorrhage. Consequently, SNC guidelines recommend its use to identify low-risk TBI patients for whom CT scans may not be necessary.[1]

Despite its diagnostic value, the efficacy of salivary S100B remains underexplored. Unlike blood sampling, saliva collection is non-invasive, requires no specialized personnel, and eliminates infection risks associated with blood products. Moreover, existing salivary diagnostics for TBI focus solely on nucleic acid detection, lacking protein-based biomarkers commonly used in neurological evaluations. Given these advantages, this study aims to compare S100B levels in serum and saliva in non-operative head injury patients at RSUP HAM between March and June 2023.[3]

METHODS

This analytical observational study adopts a cross-sectional design to evaluate S100B levels in saliva and serum simultaneously. The results from both biological fluids are statistically analyzed and compared.

The study focuses on patients with non-operative head injuries, collecting saliva and blood samples at the same time for laboratory examination. The S100B levels obtained are correlated with CT scan findings. Conducted at RSUP H. Adam Malik Medan from March to June 2023, the study encompasses all non-operative head injury patients in the hospital's neurosurgery department during this period. Using a total sampling technique, all eligible patients meeting inclusion criteria—diagnosed with non-operative head injury via laboratory and radiological assessment and providing informed consent—are included. Patients undergoing surgical intervention are excluded.

Data collection consists of primary data from laboratory and radiological evaluations and secondary data from medical records. The statistical approach varies depending on data distribution: normally distributed data are presented as mean ± standard deviation and analyzed using an independent T-test, while non-normally distributed data are expressed as median quartiles and assessed with the Mann-Whitney U test. A p-value < 0.05 indicates statistical significance. Furthermore, the ROC curve is utilized to determine the optimal cutoff for S100B levels, establishing the biomarker's sensitivity and specificity.

This research aims to provide a non-invasive diagnostic tool for assessing head injury severity by validating saliva as a viable alternative to blood for S100B measurement, potentially improving clinical decision-making and patient management.

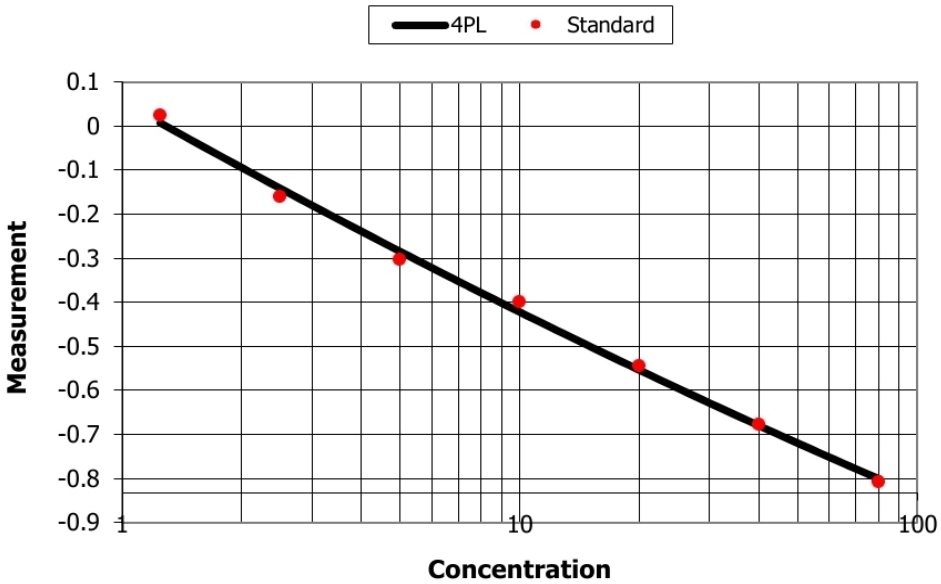
RESULTS

During the study period, 43 patients were diagnosed with head injuries at RSUP Haji Adam Malik Medan. Of these, 19 underwent surgical intervention, and 4 declined participation, leaving 20 respondents who met the inclusion criteria. This sample size is considerably lower than the required minimum of 161 participants specified in the methodology.

Table 1. Description of S100B Levels in Research Sample

S100B	Mean ± SD	Median
Serum	28,526 ± 4,061	23,265
Saliva	47,531 ± 2,852	46,31

Among the 20 respondents, serum S100B concentrations ranged from 0.69 to 62.05, with a mean of 28.526 ± 3.061 and a median of 23.265. Salivary S100B levels ranged from 13.4 to 63.98, with a mean of 47.531 ± 2.852 and a median of 46.31. Statistical analysis using the 4PL curve model, defined by the equation $y = d + (a - d) / (1 + (x/c)^b)$, yielded an R^2 value of 0.9966, indicating



that 99.66% of intracranial hemorrhage variance in non-operative brain injury cases is explained by S100B concentration variance.

Figure 1. Four Parameter Logistic Curve

Table 2. Fit Result of the 4PL Curve

a	-2,62
b	-0,1168
c	0,00061
d	6,411
MSE	0,0002444
R^2	0,9966
SS	0,001711
SYX	0,02388

These findings highlight the strong correlation between S100B levels and intracranial bleeding, reinforcing the potential of S100B as a biomarker for brain injury assessment. The significantly higher salivary S100B levels compared to serum levels further suggest the feasibility of using saliva as a non-invasive alternative for evaluating traumatic brain injuries. However, the limited sample size remains a constraint, necessitating further studies with larger cohorts to validate these preliminary findings and refine clinical applications of S100B in head injury management.

DISCUSSION

S100B is a calcium-binding protein that relays signals from cell surface receptors to intracellular targets. It is primarily expressed in astrocytes, oligodendrocytes, and Schwann cells but is also found in non-neural tissues such as chondrocytes, adipocytes, and melanocytes. In healthy adults, the median serum concentration of S100B is approximately 0.05 µg/L. The protein has five intracellular functions, including regulating protein kinase-mediated phosphorylation, modulating enzymatic activity, maintaining cell shape and motility, influencing signal transduction pathways, and promoting calcium homeostasis. At low concentrations (nanomolar levels), S100B supports neuronal survival and growth. However, at higher concentrations (micromolar levels), it induces neuroinflammation by increasing the expression of pro-inflammatory cytokines like interleukin-6 (IL-6) and promoting neuronal apoptosis.[4,5]

Clinically, S100B is the only validated biomarker with a defined cut-off value for mild traumatic brain injury (TBI). The Scandinavian Neurotrauma Committee recommends a cut-off of 0.10 µg/L within six hours post-trauma to rule out significant traumatic intracranial hemorrhage in adult patients without risk factors. This approach can significantly reduce unnecessary CT scans, minimizing healthcare costs and logistical burdens. However, the specificity of S100B is relatively low in patients with moderate-to-severe trauma, as injuries beyond the brain, such as fractures and thoracic trauma, also contribute to elevated serum S100B levels. Muller et al. found that head injuries played a minor role in increasing serum S100B in multiple trauma cases, whereas normal S100B levels were predictive of lower in-hospital mortality and overall trauma severity.[6]

A systematic review of 2,082 patients found that an S100B cut-off of 0.10 µg/L was sufficiently safe for excluding intracranial injury. Seidenfaden et al. further demonstrated that pre-hospital S100B levels measured 45 minutes post-trauma averaged 0.29 µg/L, while hospital-based levels measured 108 minutes post-trauma averaged 0.17 µg/L. The study found 100% sensitivity and a negative predictive value of 100% for detecting intracranial lesions when serum S100B exceeded 0.10 µg/L, confirming its utility in ruling out serious brain injuries. However, early testing before peak levels (within 1-3 hours post-injury) risks low sensitivity and high false-negative rates.[7,8]

Aging also influences S100B expression. Charlotte et al. observed that serum S100B concentrations increase with age, with median levels of 0.18 µg/L in individuals aged 65-79 years**,** 0.26 µg/L in those 80-89 years, and 0.32 µg/L in patients over 90 years. The study suggested age-adjusted cut-offs (0.11-0.15 µg/L) to enhance specificity while maintaining 100% sensitivity. Additionally, Sheng et al. found that cortical S100B expression correlates with β-amyloid plaque accumulation in elderly brains, potentially contributing to neurodegeneration through inflammatory astrocyte activation.[9,10]

Recent studies highlight the diagnostic potential of salivary S100B**.** Janigro et al. found that salivary S100B levels were 3.9 times higher than serum levels, with a strong correlation (Pearson's $r = 0.79$, $p < 0.01$). Salivary S100B was equally effective in distinguishing TBI patients from controls (AUC = 0.75, compared to serum AUC = 0.94). Yeung et al. also reported significantly elevated salivary S100B in pediatric TBI patients (113.2 pg/mL vs. 18 pg/mL, $p = 0.021$**)**, suggesting its potential use in children.[1,11]

Given its non-invasive**,** cost-effective, and rapid diagnostic capabilities, salivary S100B could revolutionize early TBI detection, eliminating the need for centrifugation, specialized storage, or invasive sampling, thus streamlining clinical workflows.

CONCLUSION

S100B is a crucial biomarker for traumatic brain injury, aiding diagnosis through serum and saliva testing. Salivary S100B offers a non-invasive, cost-effective alternative, enhancing early detection and reducing unnecessary CT scans.

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