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Article

The Diagnostic Value of Ubiquitin C-Terminal Hydrolase L1 (UCH-L1) and Progranulin (PGRN) Markers Compared to Some of the Traditional Laboratory Markers in Spinal Cord Injury: A Case-Control Study

Mustafa Alburhan[1], Muataz Mohammed Al-Taee*[2], Ahmed Muzahem shallal Al-Ani[3]

1. Department of Medical Chemistry, College of Medicine, Al-Mustansiriyah University, Baghdad, Iraq
2. Department of Biotechnology, College of Science, University of Baghdad, Baghdad, Iraq
3. Department of biology, college of science, University of Baghdad, Baghdad, Iraq

*Correspondence : mutaz.mohammed@sc.uobaghdad.edu.iq

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Abstract: Background: Spinal cord injury (SCI) is considered one of the most functionally and clinically devastating traumatic neurological injuries, and there is still a need to have blood biomarkers that can be used to aid in early evaluation and enhance diagnostic distinction. Ubiquitin C-Terminal Hydrolase L1 (UCH-L1) is a neurogenic injury marker and progranulin (PGRN) is an inflammatory, cell survival, and neural repair molecule. **Objective:** The objective of the study was to assess the diagnostic usefulness of both UCH-L1 and PGRN in patients with spinal cord injury, and compare them with a healthy control group, and their correlation with common clinical and laboratory markers. **Methods:** The study was conducted using a case-control design and included 120 participants: 60 patients with spinal cord injury and 60 controls. UCH-L1 and PGRN were measured by ELISA, along with a number of routine laboratory variables. Medians and interquartile ranges were used to present the data, the Mann-Whitney U test for comparisons between the two groups, and ROC analysis to assess diagnostic performance, with a statistical significance level of <0.05. **Results:** No statistically significant differences were observed between the two groups regarding age and body mass index ($p=0.07$ and $p=0.087$, respectively), supporting the similarity of baseline characteristics. In contrast, patients showed marked increases in CK, LDH, CRP, WBC, and glucose, along with a significant decrease in Hb, all with high statistical significance ($p<0.001$). PGRN was also significantly elevated in patients compared to controls (203.76 vs. 113.8, $p<0.001$), as was UCH-L1 (86.4 vs. 39.7, $p<0.001$). The severity distribution showed that 78.3% of cases were in the severe category. In the correlation analysis, a strong positive correlation was observed between UCH-L1 and CK (rho = 0.900, p = 0.04), while the relationship between PGRN and CRP was marginally significant (rho = 0.890, p = 0.05). The ROC analysis showed that PGRN had the highest discriminatory power (AUC=0.99, sensitivity 0.93, specificity 1.00, at a cutoff of 158.1), followed by LDH (AUC=0.97) and then UCH-L1 (AUC=0.957), with WBC, CRP, and CK also performing well. **Conclusions:** The analysis shows

a unique blood profile of spinal cord injury that is a combination of neuropathic injury, inflammatory, and tissue damage markers. PGRN was the most promising exploratory biomarker to differentiate between patients and healthy controls in this sample, and UCH-L1 was found to have high diagnostic value that is more directly related to the neuropathic injury component. The findings indicate that a multi-marker diagnostic method can be more practical compared to the use of a single marker, especially in the initial evaluation of cases.

Keywords: Spinal cord injury, Progranulin (PGRN), Ubiquitin C-Terminal Hydrolase L1 (UCH-L1) and neurochemical markers.

Introduction

Spinal cord injury (SCI) is a traumatic neurological condition with a significant clinical and functional burden, as it results in motor and sensory deficits and autonomic disorders whose effects may extend beyond the acute phase, with clear implications for quality of life and the health and social burden [1]. According to the World Health Organization, over 15 million individuals across the globe live with a spinal cord injury and that a large percentage of these injuries are caused by trauma, especially falls, road accidents, and violence [2].

Although significant progress has been made in imaging and clinical evaluation, biomarkers that can aid in early diagnosis, enhance the determination of injury severity, and predict outcomes are still needed [3]. Two of the most basic pillars of traditional assessment are neurological examination and radiological imaging, which is admittedly the most basic, but in certain instances, their practical accuracy can be undermined by the time of the assessment, the presence of concomitant injuries, and the inability to completely evaluate neural tissue damage at the initial stages [4]. Thus, recent studies have resorted to the examination of blood biomarkers as auxiliary tools that can reflect the elements of nerve injury and the systemic inflammatory reaction after injury [5].

UCH-L1 is a neurotrophic protein, which has attracted growing interest over the last several years, as it is closely related to neurons and plays a role in protein balance in the neuronal cell [6]. This protein may be discharged into the circulation when neurons are injured, and thus it is a viable biological marker to identify acute neuronal damage [7]. A clinical trial of traumatic spinal cord injury patients revealed that serum UCH-L1 levels were elevated in patients than in healthy controls, and it may be associated with the severity of injury and clinical outcome, which indicates its usefulness as a promising biomarker in this scenario [8].

Progranulin (PGRN), in its turn, is a multifunctional molecule, the functions of which overlap with the regulation of inflammation, cell survival, and neural repair processes.. Although its presence in the clinical literature on spinal cord injury remains less prominent than that of some other markers, experimental studies have yielded significant findings; it has been shown that PGRN deficiency may exacerbate spinal cord injury by promoting inflammation and cell death, while its upregulation may be associated with improved functional recovery and a shift in the microglial response toward a more anti-inflammatory phenotype [9]. These findings provide a plausible biological basis for studying PGRN as a potential biomarker in spinal cord injury, particularly when compared to biomarkers reflecting direct neural injury such as UCH-L1 [10].

Despite growing interest in biomarkers for spinal cord injury, a knowledge gap remains regarding human studies investigating the comparative diagnostic performance of neurogenic and inflammatory biomarkers, particularly in clinical settings that require easy-to-apply and early-use tools [11]. Hence the importance of studying UCH-L1 and PGRN together, alongside some traditional laboratory markers, to assess their ability to distinguish between patients and healthy individuals and to determine their relationship with relevant clinical characteristics [12].

Accordingly, this case-control study aimed to evaluate the diagnostic performance of both UCH-L1 and PGRN in patients with spinal cord injury, compare them with a healthy control group, investigate their relationship with certain clinical and laboratory markers, and to explore their utility as potential biomarkers in this field.

Methodology

This study was conducted as a case-control study to evaluate the diagnostic value of both UCH-L1 and Progranulin, along with a number of common laboratory markers, in patients with spinal cord injury, and to compare these findings with those of a healthy control group. Blood samples were collected from SCI patients within 12 hours after injury during the study period.

Study Design and samples

This is a case-control study conducted Dr. Saad Al Watri Hospital for Neurological Sciences and Al-Imameen Al-Kadhmain Medical City, Baghdad, Iraq, between December 2025 and April 2026. The study included patients clinically and/or radiologically diagnosed with spinal cord injury, along with a control group of healthy individuals or those without this condition.

Participants and Sample Size

The sample consisted of two groups: a case group comprising (60) patients with spinal cord injury, and a control group comprising (60) healthy participants. Participants were selected according to predefined inclusion and exclusion criteria.

•Inclusion criteria for the case group: included patients clinically and/or radiologically diagnosed with spinal cord injury.

•Exclusion criteria for the case group:

- The presence of severe chronic diseases that may affect the parameters under study, such as liver or kidney disease
- The use of medications, such as anti-inflammatory drugs, steroids, antidiabetic medications
- A history of severe neurological or systemic conditions.
- Incomplete clinical, demographic, or laboratory data for the participant.

Ethics Approval

The research protocol numbered 51/2026 was reviewed and approved by the appropriate ethical body within the Iraqi Ministry of Health, specifically by the Research Committee of the National Centre for Training and Human Development, following standard procedures. Prior to their participation, all individuals provided written informed consent, or such consent was acquired from their guardians when necessary.

Sample Collection and Laboratory Assays

Venous blood samples were collected from all participants under conditions that were as standardized as possible, blood samples were collected within 12 hours after injury, serum was then separated and stored at [- 20] °C until analysis. Both UCH-L1 and Progranulin (PGRN) were measured using the Enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions (Thermo fisher scientific USA). Conventional laboratory markers were measured using a Promega GloMax Discover analyze.

Statistical methods

Statistical analysis was performed using (SPSS version 27, MedCalc and GraphPad Prism 10). After reviewing the data distribution, continuous variables were presented as the median and interquartile range (IQR), and categorical variables were presented as the number and percentage (n (%)). The Mann–Whitney U test was used to compare two independent groups for non-normal continuous variables, and the chi-square test or Fisher's exact test was used as appropriate to analyze categorical variables. To evaluate diagnostic performance, ROC curves were plotted for each variable separately, and the area under the curve (AUC) was calculated with a 95% confidence interval; the optimal cutoff point was determined using the Youden index, and sensitivity and specificity were calculated. Statistical significance was set at a p-value of less than 0.05.

Results

The current study's findings regarding differences between SCI patients and the control group, focusing on clinical and laboratory variables, as well as evaluating the significance of certain

biomarkers in diagnosing the condition. The findings revealed that there were significant differences between the two groups in several indicators, especially CK, glucose, WBC, Hb, LDH, and CRP, and that PGRN and UCH-L1 levels were significantly higher in patients than in the control group. The findings also revealed that the majority of the cases of SCI were severe, which is indicative of the type of injury in the sample. Correlation analyses were also performed between some of the biomarkers and other laboratory variables, as well as the diagnostic accuracy of the biomarkers was evaluated with the help of ROC curve analysis; some of the variables showed high discriminatory power, which can justify their usefulness in diagnosis. Overall, the results of this section provide a clear picture of the biochemical and clinical differences associated with SCI and highlight the potential importance of certain biomarkers in the clinical assessment of the condition.

There was a clear male dominance in the gender distribution of the participants in both groups. The proportion of males in the spinal cord injury group was 86.7% and the control group was 83.3% and the proportion of females in the spinal cord injury group was 13.3 and the control group was 16.7%. This distribution indicates a fair amount of similarity between the two groups in regards to gender, thereby minimizing the chances of gender being a confounding variable in the interpretation of the differences in the biomarkers under study.

Table 1. Comparison of general characterization, clinical finding and biochemical variables between SCI patients and the control group.

Variable	SCI Median (IQR), n= 60	Control Median (IQR), n= 60	P value
Age yr	35 (27.0 - 42.25)	33 (25.0 - 40.25)	0.07
BMI, kg/m²	26.5 (24.05 - 29.725)	27.7 (25.25 - 30.925)	0.087
CK, U/L	618.8 (279.028 - 715.8)	152.4 (125.925 - 169.73)	<0.001
Glucose, mg/dL	193 (102.75 - 246.287)	102 (89.75 - 121.75)	<0.001
WBC, ×10⁹/L	15.2 (11.675 - 20.24)	7.35 (5.975 - 8.6)	<0.001
Hb, g/dL	9.3 (8.5 - 10.1)	14.5 (13.5 - 15.5)	<0.001
LDH, U/L	458 (413.25 - 537.0)	139 (114.75 - 175.75)	<0.001
CRP, mg/L	22.89 (19.455 - 27.855)	5.0 (3.395 - 12.55)	<0.001
PGRN, ng/mL	203.76 (198.3 - 211.208)	113.8 (108.3 - 121.208)	<0.001
UCH-L1, ng/mL	86.4 (80.377 - 88.33)	39.7 (39.288 - 40.262)	<0.001

This table presents a comparison of variable values between the two groups. Statistically significant differences were observed in most variables, particularly CK, Glucose, WBC, Hb, LDH, CRP, PGRN, and UCH-L1.

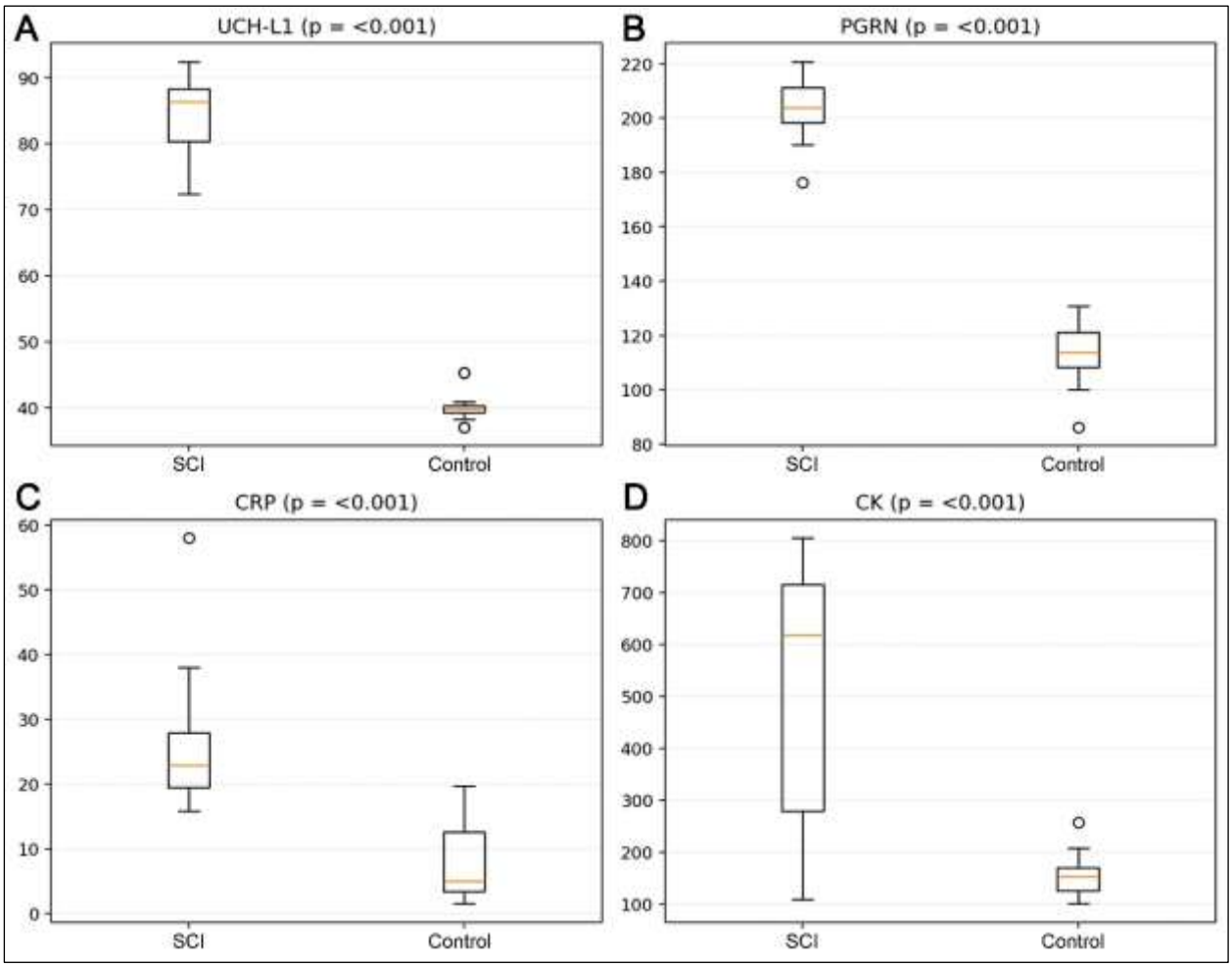

Figure 1. Box plots of UCH-L1, PGRN, CRP, and CK levels in SCI patients and the control group.

This figure shows a clear increase in UCH-L1, PGRN, CRP, and CK levels in SCI patients compared to the control group, with statistically significant differences ($p < 0.001$)

Table 2. Distribution of injury severity among SCI patients.

Severity of SCI (cases only)	
Group	**Label**
Not Severe	13 (21.7%)
Severe	47 (78.3%)

This table shows that most SCI cases fell into the Severe category compared to the Not Severe category. Figure 3 illustrates the proportion of Severe and Not Severe cases within the patient group.

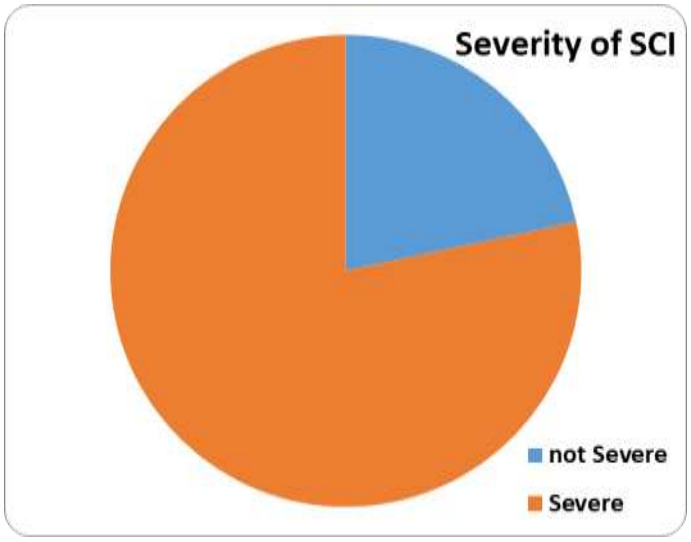

Figure 2. Graphical representation of injury severity in SCI patients.

Table 3. Correlation between UCH-L1, PGRN, and selected laboratory variables.

Anchor	Compared with	Spearman rho	P value
UCH-L1	CK	0.900	0.04
UCH-L1	Glucose	-0.189	0.149
UCH-L1	WBC	-0.058	0.660
UCH-L1	Hb	0.181	0.167
UCH-L1	LDH	0.610	0.770
UCH-L1	CRP	0.500	0.434
UCH-L1	PGRN	0.800	0.06
PGRN	CK	0.788	0.09
PGRN	Glucose	-0.197	0.131
PGRN	WBC	-0.146	0.265
PGRN	Hb	0.088	0.505
PGRN	LDH	0.790	0.488
PGRN	CRP	0.890	0.05
PGRN	UCH-L1	0.800	0.06

This table presents Spearman's rho and P-values to measure the strength and direction of the correlation between biomarkers and other variables.

Figure 3. Heatmap of the relationship between laboratory variables and biomarkers in SCI patients.

This figure illustrates the direction and strength of the correlation between the studied variables, with positive values indicating a positive correlation and negative values indicating an inverse correlation. Notably, there are strong positive correlations between UCH-L1 and CK, and between PGRN and each of CK, LDH, and CRP.

ROC curve analysis demonstrated excellent diagnostic performance for the PGRN marker, with an AUC of 0.99 at an optimal cutoff value of 158.1, followed by LDH with an AUC of 0.97 at a cutoff value of 268, and UCH-L1 with an AUC of 0.957 at a cutoff value of 64.8. WBC, CRP, and CK also demonstrated good discriminatory ability, with AUC values of 0.92, 0.91, and 0.89, respectively, at cutoff values of 10.9, 16.9, and 256.6, respectively (Table 5 and figure 5).

Table 4. Diagnostic value of biomarkers and laboratory variables according to ROC analysis.

Biomarker	AUC	Optimal cutoff	Sensitivity	Specificity
PGRN, ng/mL	0.99	158.1	0.93	1
UCH-L1, ng/mL	0.957	64.8	0.95	0.82
LDH, U/L	0.97	268	0.93	0.99
CRP, mg/L	0.91	16.9	0.85	1
CK, U/L	0.89	256.6	0.8	0.98
WBC, $\times 10^9$/L	0.92	10.9	0.9	0.98

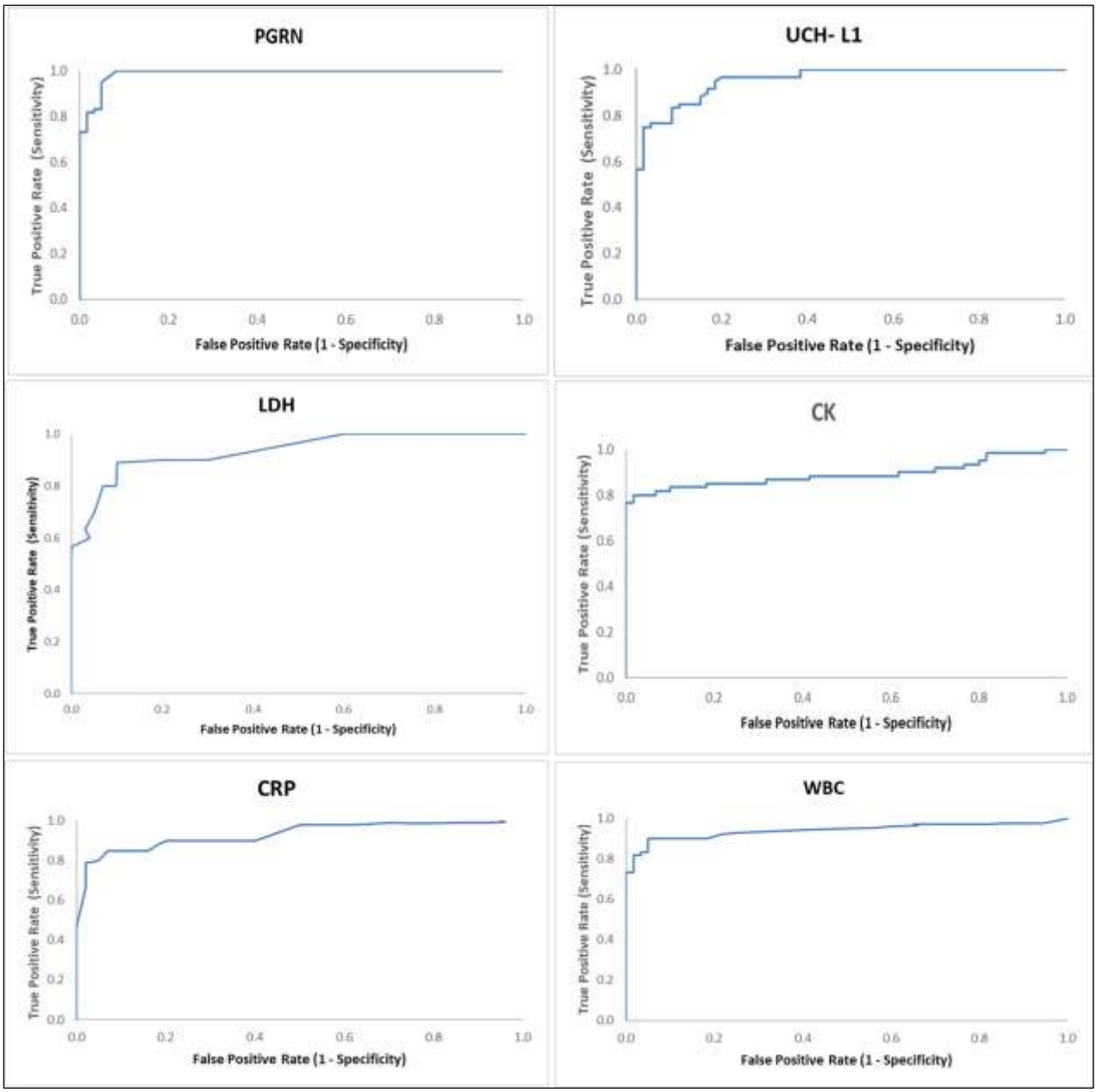

Figure 4: ROC curves for evaluating the diagnostic ability of PGRN, UCH-L1, LDH, CK, CRP, and WBC in distinguishing between SCI patients and the control group.

This chapter is based on the tables and figures included in the attached results file. The discussion follows a case-control study design, focusing on the magnitude of differences between the two groups, statistical significance, biological plausibility, and the consistency of the results with the published medical literature.

Discussion

First: General Characteristics of the Sample

The sample was similar in terms of age and body mass index (BMI) between the patients and controls because the differences were not statistically significant (age: p=0.07; BMI: p=0.087). It is a significant methodological consideration because it decreases the risk that later differences in vital signs can be attributed to differences in the baseline of the two groups and it argues in favor of the idea that the observed difference is more directly connected to the disease itself than to confounding factors. Moreover, the fact that the majority of patients are males (86.7) seems to be in line with the established epidemiology of traumatic spinal cord injury, with most clinical series indicating a higher incidence of

males because of their greater exposure to high-energy accidents and work-related and traffic-related trauma [13, 14].

Second: Significance of Routine Laboratory Findings

The findings showed extremely distinct differences between cases and controls in CK, LDH, CRP, WBC, glucose, and hemoglobin, which were very significant ($p<0.001$). This trend does not seem to be accidental but is probably a result of the intersection of several pathological pathways after injury: acute tissue injury, a systemic inflammatory response, and a metabolic imbalance related to the extent of the injury. The significant increase in CK and LDH is in keeping with the existence of widespread cellular and muscular damage and the leakage of enzymes of damaged tissues, which is also in line with the traumatic nature of spinal cord injury and the frequent associated surrounding muscular or structural injury [15,16].

High levels of white blood cells and CRP, conversely, are typical of the initial inflammatory reaction after spinal cord trauma, which is not confined to the injury location but spreads throughout the body and can be related to the extent of the trauma and the ensuing complications [17]. Recent human research has indicated that early white blood cell alterations have prognostic worth to functional recovery, and a big clinical trial of the CRP-to-albumin ratio indicated that inflammatory markers at admission could be used to aid in evaluating severity and prognosis [16,20]. Therefore, high WBC and CRP in our patients are not just the accidental laboratory results but seem to be included in the initial biological signature of injury [18, 19].

Moreover, the significant increase in the glucose levels in patients relative to controls is in line with the idea of post-traumatic hyperglycemia after neurotrauma. A study using NASCIS-3 data indicated that hyperglycemia during the hyperacute period after spinal cord injury could be linked to poorer outcomes, which supports the idea that glucose is not a secondary variable but may be the measure of the intensity of physiological stress and potentially a factor that promotes secondary injury [20]. Conversely, hemoglobin was much lower in patients, which can be attributed to blood loss, comorbid trauma, volume loss, and, perhaps, the development of an inflammatory reaction. This decrease is especially important since the literature indicates that the increased levels of Hb at the initial stage can be linked to an improved likelihood of neurological recovery [21].

Third: UCH-L1 as a marker of neurological injury

The research showed that the UCH-L1 levels in patients were significantly higher than the controls with a median of 86.4 and 39.7 respectively and a highly significant statistical p-value ($p<0.001$). This observation is one of the most consistent with the biological background of the marker; UCH-L1 is a neurogenic protein that is linked with neuronal and axonal damage. Human case-control study has shown that serum UCH-L1 levels were much greater in traumatic spinal cord injury and correlated with greater severity and worse subsequent recovery [22]. A second study of cerebrospinal fluid showed that UCH-L1 has potential to differentiate the severity of injury and outcome during the initial few hours after trauma [23].

Practically, our results indicate that the AUC of 0.957 at a cutoff of 64.8 places UCH-L1 in the group of markers with excellent diagnostic performance. It is also interesting to note that the high sensitivity (0.95) was achieved at the cost of reduced specificity relative to PGRN and LDH, but it was still good (0.82), which makes this marker appealing in situations when the risk of false negativity must be reduced to the minimum. This observation is in line with the recent literature that UCH-L1 is among the most promising neurological markers, but its actual utility is enhanced when used in combination with other markers as opposed to when used alone [24].

Fourth: PGRN Between Inflammatory Significance and Diagnostic Value

The elevation in PGRN was even more pronounced than that of UCH-L1; its median value was 203.76 in patients versus 113.8 in controls, with highly significant results ($p<0.001$). From a mechanistic perspective, this result appears plausible, as progranulin is associated with the regulation of inflammation, cell survival, and immune modulation within neural tissue. Experimental studies have shown that PGRN deficiency increases spinal cord injury by promoting inflammation and apoptosis, whereas its administration improves functional recovery and promotes a shift in the microglial phenotype toward an anti-inflammatory state **[25].** Therefore, its elevation in our patients can be

understood as a response accompanying acute injury and a compensatory attempt to limit secondary injury.

Most importantly, PGRN achieved the best performance among all studied variables in ROC analysis, with an AUC of 0.99 at a cutoff of 158.1, demonstrating near-perfect specificity and high sensitivity. This level of discrimination is rare in clinical studies and suggests that PGRN may be a strong candidate for laboratory-assisted diagnosis in a case-control model. However, this result should be treated with scientific caution; because excessively high performance in medium-sized samples may partly reflect sample specificity or the absence of external validation. Therefore, the true value of PGRN can only be determined after testing it in independent, multicenter samples. Nevertheless, the current result remains highly significant because it provided this marker with the best balance between sensitivity and specificity in the study.

Fifth: Disease Severity and Sample Distribution

The results showed that 78.3% of cases fell into the severe category, compared to only 21.7% in the non-severe category. This distribution partly explains the marked elevation in inflammatory, neurological, and enzymatic markers; because the predominance of severe cases often increases the overall biological burden of secondary injury. It is also consistent with the notion that referral centers receive a higher proportion of complex cases, which may limit the generalizability of the absolute values of the markers to all patients, but does not negate the significance of the directional differences between cases and controls. Overall, the consistency between the prevalence of severe cases and elevated vital signs supports rather than undermines the clinical significance of the findings.

Sixth: Interpreting the Correlations Between Biomarkers and Routine Variables

In the correlation analysis, a strong positive correlation emerged between UCH-L1 and CK (rho=0.900, p=0.04), and a marginal positive correlation was observed between PGRN and CRP (rho=0.890, p=0.05). These two relationships suggest that UCH-L1 may move in parallel with the severity of general tissue damage, while PGRN moves more closely along the inflammatory axis. This interpretation is biologically consistent with the neurogenic nature of UCH-L1 and the immunoregulatory nature of PGRN. However, the remaining correlations, although some showed high rho values, were not statistically significant; therefore, they should not be interpreted as having significant causal or inferential meaning. This variability most likely reflects the effect of the limited sample size, temporal heterogeneity in sample collection, or the presence of clinical heterogeneity within the case group.

Thus, it can be said that the correlation analysis in this study was useful in suggesting the biological trends of the relationship between biomarkers, but it was not sufficient to determine the network of relationships among them. This is common in biomarker research for spinal cord injury, as recent reviews confirm that predictive value improves when biomarkers are studied across multiple panels and at serial time points, rather than in a single isolated measurement **[26].**

Seventh: Clinical Value of ROC Analysis

Clinically, the ROC analysis showed that PGRN, LDH, and UCH-L1 had the highest discriminatory power, followed by WBC, CRP, and CK. This finding puts the study in a significant practical setting; it does not just indicate that there are statistical differences but also indicates how far each variable can differentiate between patients and healthy individuals. All statistically significant differences do not necessarily translate into diagnostic utility, but the three best markers obviously passed this test. In particular, the fact that the AUC of both PGRN and LDH approaches the ideal value of one implies that both of these variables have a high ability to be accurately classified in this sample.

However, a more prudent reading must mention that the case-control design is inherently biased towards overestimating diagnostic performance in cases where groups are distinctly different, unlike in clinical practice where borderline cases and overlapping diagnostic diagnoses are present. Thus, the findings may be considered as good indicators of diagnostic potential at first sight, but they cannot substitute prospective validation research that will test these cutoffs in more realistic and extensive clinical conditions.

Summary of Discussion

This study demonstrates that spinal cord injury has a unique laboratory, immunological, and neurological signature that is detectable in blood. CRP, WBC, LDH, CK, glucose, and Hb were found to be useful as routine markers to reflect the burden of injury and systemic response, whereas UCH-L1 and PGRN were found to be more specific to neurological injury and inflammatory regulation. PGRN was the most appropriate diagnostic marker within the confines of this sample, and UCH-L1 was a good indication of concomitant neuropathic injury. The partial correlations with CK and CRP confirm the notion that neuropathic markers do not act independently of the inflammatory and tissue environment, but instead, they interact with it. The optimal interpretation of the study findings, therefore, does not lie in the search of a single, ideal, marker, but the suggestion of an integrated panel of neurogenic, inflammatory, and enzymatic markers to enhance the early diagnosis of spinal cord injury.

Conclusions

This research suggests that UCH-L1 and progranulin could be useful in the diagnosis of patients with spinal cord injury because they demonstrated significant differences between cases and controls and high discriminatory ability in ROC analysis. This finding is in line with a clinical study that provided human evidence on UCH-L1 in traumatic spinal cord injury that reported a significant increase in its serum levels with injury severity and later neurological outcomes.

Moreover, the fact that Progranulin is especially prominent in the present sample is especially noteworthy because the direct clinical evidence on it is not as widespread as it is the case with certain other neurotrophins. However, experimental evidence indicates that it has a strong biological foundation to its action; animal models have demonstrated that Progranulin deficiency worsens spinal cord injury by enhancing inflammation and cell death, and its administration or upregulation has been linked to better functional recovery and a change in the glial response to a more anti-inflammatory pattern. In this way, the present discovery does not seem to be detached of the biological background of this molecule but rather in line with it.

Conversely, the high WBC, CRP, and enzyme levels in the patient group confirm the notion that spinal cord injury is not confined to local neural damage but is also accompanied by a quantifiable systemic inflammatory reaction in the blood. This opinion has been reinforced by recent reviews that have demonstrated that peripheral blood markers, especially white blood cells and their derivatives, can be used to stratify patients and to assess their prognosis. A recent multicenter study also showed that the combination of inflammatory markers and structural or radiological data could enhance the severity assessment and predict neurological outcome.

Based on these results, the present study advocates a multi-component diagnostic model which integrates direct neurological markers with conventional inflammatory markers instead of using a single variable. This finding aligns with recent systematic reviews that have found that the biomarker landscape in spinal cord injury is changing towards composite models that are more likely to explain clinical heterogeneity and predict outcomes.

According to the above, the most important research result is that UCH-L1 is a good candidate marker of neuropathic injury, and Progranulin is a marker of high potential value that needs further clinical validation. Moreover, the integration of these markers with conventional inflammatory markers can provide more stability and a wider practical applicability to the diagnostic model, especially at the initial stages of patient assessment.

Limitations

There are a number of limitations to this study. To begin with, the case-control design may overestimate the diagnostic potential of the biomarkers in a real-life clinical scenario. Second, the sample was moderate and in two centers only, which may limit the generalization of the results. Third, the biomarkers were not measured at various time points after injury and therefore, their dynamic change patterns cannot be deduced. Fourth, the cutoff values obtained through the ROC analysis need to be validated externally and then be implemented in clinical practice.

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