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ORIGINAL ARTICLE

Galectin-3 as a Novel Biomarker for Predicting Clinical Outcomes in Hospitalized COVID-19 Patients

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SUMMARY

Background: **Galectin-3 has been shown to play a key pathophysiological role in pulmonary associated inflammatory response and lung fibrosis in COVID-19 and is a mediator for viral adhesion. However, there is limited data about its potential role in severity and prognosis of COVID-19. This study aimed to investigate the predictive role of serum galectin-3 concentrations in the severe clinical outcomes of hospitalized COVID-19 patients: the severity of pneumonia, in-hospital mortality, and the need for intensive care unit (ICU) admission.**

Methods: **This single-center study included 68 patients with laboratory- and radiologically-confirmed COVID-19 admitted to our emergency department. The study population was divided into patients with primary clinical outcomes (n = 32) and those without (n = 36). The need for ICU admission and/or in-hospital mortality were the primary clinical endpoints. The study group was also classified based on pneumonia severity: severe or mild/moderate. Blood samples were collected within 48 hours of admission to estimate serum galectin-3 concentrations.**

Results: **Multivariate regression analysis showed that lower concentrations of galectin-3 and arterial oxygen saturation (SpO_2) were independently associated with the primary clinical outcomes (OR = 0.951, p = 0.035; OR = 0.862, p = 0.017, respectively); increased concentrations of galectin-3 were an independent predictor of severe pneumonia (OR = 1.087, p = 0.016). In the receiver operating characteristics curve analysis, serum galectin-3 concentrations at hospital admission predicted pneumonia severity with 52.1% sensitivity and 90% specificity with a cutoff of 38.76 ng/mL.**

Conclusions: **Circulating galectin-3 at hospital admission could be a useful biomarker for identifying COVID-19 patients at high risk for severe pneumonia.**

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Supplementary Data

Table S1. Laboratory findings, treatments, and adverse events during hospitalization of the study participants based on pneumonia severity.

	Total Patients (n = 68)	Severe Pneumonia (n = 48)	Mild/Moderate Pneumonia (n = 20)	p-value
Laboratory findings (peak levels during hospitalization)				
Fasting Plasma Glucose (mg/dL)	226 (93 - 710.4)	230.85 (98 - 710)	158.15 (93 - 415)	0.012 *
BUN (mg/dL)	30.14 (8.13 - 167.99)	36.8 (16.9 - 168)	20.23 (8.13 - 48.46)	< 0.001 *
Creatinine (mg/dL)	1.65 ± 1.9	2.03 ± 2.46	1.09 ± 0.3	0.022 *
CKD-EPI (mL/min/1.73 m^2)	96.03 ± 25.9	94.67 ± 28.3	98.05 ± 15.4	0.529
Urea (mg/dL)	63.7 (17.4 - 359.5)	77.05 (36.10 - 359.5)	43.3 (17.4 - 103.7)	< 0.001 *
Uric acid (mg/dL)	6.41 ± 2.5	6.86 ± 2.6	5.42 ± 1.6	0.038 *
Sodium (mmol/L)	143.5 ± 6.7	144.4 ± 7.2	141 ± 3.9	0.034 *
Potassium (mmol/L)	5.34 ± 0.5	5.39 ± 0.6	5.15 ± 0.5	0.114
AST (IU/L)	68 (17 - 2,394)	67 (17.5 - 2,394)	62.5 (17 - 1,145)	0.156
ALT (IU/L)	70.1 (15.6 - 1,057)	70.7 (18 - 1,057)	54 (15.6 - 172)	0.244
LDH (IU/L)	470 (165 - 4,131)	518 (210 - 4,131)	325 (165 - 612)	< 0.001 *
CRP (mg/L)	132.7 (3.11 - 383)	148.55 (3.11 - 383)	69.44 (0.38 - 254.19)	0.001 *
D-dimer (µg/L)	3,123 (189.4 - 43,730)	5,515.8 (189.4 - 43,730)	1,650 (190 - 7,082)	0.001 *
Ferritin (ng/mL)	1,136 (25.72 - 71,513)	1,167 (87.5 - 71,513)	845.35 (25.72 - 6,172)	0.239
Hs-TnT (pg/mL)	13.5 (3 - 764)	19.85 (3 - 764)	8.73 (3 - 39.61)	0.002 *
Pro-BNP (pg/mL)	709.2 (81.08 -35,000)	1,184.1 (110.3 - 35,000)	336.35 (81.08 - 3,897.2)	< 0.001 *
Procalcitonin (ng/mL)	0.27 (0.04 - 44.63)	0.41 (0.04 - 7.59)	0.13 (0.04 - 44.63)	0.002 *
Fibrinogen (mg/dL)	747 (316 - 1,200)	761 (316 - 1,200)	638.5 (283.7 - 920)	< 0.001 *
Albumin (g/dL)	3.86 ± 0.5	3.8 ± 0.5	3.93 ± 0.6	0.139
Hgb (gr/dL)	13 ± 2.1	13.08 ± 2	12.78 ± 2.3	0.888
Hematocrit (%)	38.04 ± 5.9	38.07 ± 5.5	37.78 ± 6.9	0.856
WBC (10^3/µL)	15.64 ± 8.7	17.97 ± 8.6	10.14 ± 5.8	< 0.001 *
RBC (10/µL)	4.41 ± 0.7	4.45 ± 0.6	4.41 ± 0.8	0.830
Neutrophil (10^3/µL)	11.6 (1.6 - 49.6)	14.95 (3.7 - 49.6)	6.8 (1.6 - 26.7)	< 0.001 *
Lymphocyte (10^3/µL)	1.9 (0.3 - 6.1)	2 (0.3 - 6.1)	1.9 (0.3 - 4)	0.676
Lymphocyte (%)	25.48 ± 11.4	24.78 ± 12.1	27.6 ± 8.9	0.164
Neutrophil (%)	88.87 ± 8.2	92.25 ± 4.8	78.93 ± 12	< 0.001 *
Platelet (10^3/µL)	450 (55 - 961)	478 (151 - 759)	336.5 (55 - 961)	0.010*
Treatment				
Azithromycin, n (%)	2 (2.9%)	2(4.2%)	0 (0%)	1.000
Favipiravir, n (%)	67 (98.5%)	47 (97.9%)	20 (100%)	1.000
Heparin, LMWH, n (%)	65 (95.6%)	48 (100%)	17 (85%)	0.023 *
Dipyridamole, n (%)	18 (26.5%)	16 (33.3%)	2 (10%)	0.047 *
Steroid, n (%)	60 (88.2%)	47 (97.9%)	13 (65%)	0.001 *
Immune modulator, n (%)	8 (11.8%)	8 (16.7%)	0 (0%)	0.094
Antibiotics, n (%)	50 (73.5%)	39 (81.3%)	11 (55%)	0.025 *
Inotrope, n (%)	8 (11.8%)	8 (16.7%)	0 (0%)	0.094
ASA, n (%)	25 (36.8%)	23 (47.9%)	2 (10%)	0.003 *
P2Y12 inhibitor, n (%)	4 (5.9%)	3 (6.3%)	1 (5%)	1.000
Beta blocker, n (%)	15 (22.1%)	13 (27.1%)	2 (10%)	0.199

Table S1. Laboratory findings, treatments, and adverse events during hospitalization of the study participants based on pneumonia severity (continued).

	Total Patients (n = 68)	Severe Pneumonia (n = 48)	Mild/Moderate Pneumonia (n = 20)	p-value
CCB, n (%)	12 (17.6%)	11 (22.9%)	1 (5%)	0.094
RAS blocker, n (%)	13 (19.1%)	10 (20.8%)	3 (15%)	0.741
Diuretic, n (%)	23 (33.8%)	22 (45.8%)	1 (5%)	0.001 *
Statin, n (%)	5 (7.4%)	5 (10.4%)	0 (0%)	0.311
Oxygen treatment via face mask, n (%)	33 (48.5%)	15 (31.3%)	18 (90%)	< 0.001 *
NIMV/HFNC, n (%)	22 (32.4%)	20 (41.7%)	2 (10%)	
Orotracheal intubation, n (%)	13 (19.1%)	13 (27.1%)	0 (0%)	
Adverse events during hospitalization				
Acute renal failure, n (%)	24 (36.4%)	22 (45.8%)	2 (11.1%)	0.009 *
Acute liver failure, n (%)	38 (57.6%)	28 (58.3%)	10 (55.6%)	0.839
Cerebrovascular accident, n (%)	3 (4.6%)	3 (6.5%)	0 (0%)	0.550
Myocardial injury, n (%)	31 (47.7%)	29 (63%)	2 (10.5%)	< 0.001 *

Abbreviations: BUN - blood urea nitrogen, CKD-EPI - estimated glomerular filtration rate, AST - aspartate transaminase, ALT - alanine transaminase, LDH - lactate dehydrogenase, CRP - C reactive protein, Hs-TnT - high-sensitivity troponin T, Pro-BNP - prohormone B-type natriuretic peptide, Hgb - hemoglobin, WBC - white blood cell, RBC - red blood cell, LMWH - low molecular weight heparin, ASA - acetyl salicylic acid, CCB - calcium channel blocker, RAS - renin angiotensin system, NIMV - non invasive mechanical ventilation, HFNC - high flow nasal cannula.

Table S2. Laboratory findings, treatments, and adverse events during hospitalization of the patients with and without primary composite endpoint.

	Total patients (n = 68)	Patients with primary composite end-point (n = 32)	Patients without primary composite endpoint (n = 36)	p-value
Laboratory findings (peak levels during hospitalization)				
Fasting Plasma Glucose (mg/dL)	226 (93 - 710.4)	234.75 (156 - 485)	216.6 (93 - 710)	0.147
BUN (mg/dL)	30.14 (8.13 - 167.99)	39.41 (14.53 - 167.99)	25.75 (8.13 - 122.57)	0.001 *
Creatinine (mg/dL)	1.65 ± 1.9	1.28 (0.66 - 9.41)	1.12 (0.62 - 13.9)	0.170
CKD-EPI (mL/min/1.73 m^2)	96.03 ± 25.9	101.63 ± 24	90.36 ± 25.3	0.176
Urea (mg/dL)	63.7 (17.4 - 359.5)	84.35 (31.1 - 359.5)	54.3 (17.4 - 262.3)	< 0.001 *
Uric acid (mg/dL)	6.41 ± 2.5	6.78 ± 2.4	6.12 ± 2.4	0.277
Sodium (mmol/L)	143.5 ± 6.7	146.06 ± 8	141.06 ± 3.6	0.003 *
Potassium (mmol/L)	5.34 ± 0.5	5.44 ± 0.6	5.21 ± 0.6	0.103
AST (IU/L)	68 (17 - 2,394)	68.2 (24.3 - 2,394)	57.9 (17 - 1,145)	0.103
ALT (IU/L)	70.1 (15.6 - 1,057)	70.7 (20 - 1,057)	64.75 (15.6 - 382.6)	0.324
LDH (IU/L)	470 (165 - 4,131)	538 (325 - 4,131)	388 (165 - 714)	< 0.001 *
CRP (mg/L)	132.7 (3.11 - 383)	173.33 (18.07 - 383)	113.8 (0.38 - 275.5)	0.002 *
D-dimer (µg/L)	3,123 (189.4 - 43,730)	7,300 (189.4 - 43,730)	1,965 (290 - 24,114)	0.001 *
Ferritin (ng/mL)	1,136 (25.72 - 71,513)	1,237 (25.72 - 71,513)	1,080.5 (26.93 - 6,172)	0.195
Hs-TnT (pg/mL)	13.5 (3 - 764)	43.12 (3 - 764)	9.56 (3 - 463.2)	< 0.001 *
Pro-BNP (pg/mL)	709.2 (81.08 - 35,000)	1,744 (110.3 - 35,000)	547.85 (81.08 - 10,374)	0.001 *
Procalcitonin (ng/mL)	0.27 (0.04 - 44.63)	0.49 (0.06 - 7.59)	0.16 (0.04 - 44.63)	0.011 *
Fibrinogen (mg/dL)	747 (316 - 1,200)	747 (437 - 1,200)	719 (283.7 - 976)	0.008 *

Table S2. Laboratory findings, treatments, and adverse events during hospitalization of the patients with and without primary composite endpoint (continued).

	Total patients (n = 68)	Patients with primary composite end-point (n = 32)	Patients without primary composite endpoint (n = 36)	p-value
Albumin (g/dL)	3.86 ± 0.5	3.74 ± 0.5	3.91 ± 0.4	0.015 *
Hgb (gr/dL)	13 ± 2.1	13.39 ± 2.1	12.64 ± 2	0.135
Hematocrit (%)	38.04 ± 5.9	38.81 ± 5.5	37.25 ± 6.2	0.277
WBC (10^3/µL)	15.64 ± 8.7	18.65 (4.5 - 54.8)	11.25 (2.1 - 28.9)	0.001 *
RBC (10/µL)	4.41 ± 0.7	4.52 ± 0.6	4.36 ± 0.7	0.327
Neutrophil (10^3/µL)	11.6 (1.6 - 49.6)	15.3 (3.7 - 49.6)	8.9 (1.6 - 26.7)	0.001 *
Lymphocyte (10^3/µL)	1.9 (0.3 - 6.1)	2.05 (0.3 - 6.1)	1.9 (0.3 - 4)	0.461
Lymphocyte (%)	25.48 ± 11.4	25.73 ± 13	25.49 ± 9.7	0.902
Neutrophil (%)	88.87 ± 8.2	92.91 ± 4.6	84.26 ± 11.2	< 0.001 *
Platelet (10^3/µL)	450 (55 - 961)	452.5 (151 - 711)	429 (55 - 961)	0.894
Treatment				
Azithromycin, n (%)	2 (2.9%)	1 (3.1%)	1 (2.8%)	1.000
Favipiravir, n (%)	67 (98.5%)	31 (96.9%)	36 (100%)	0.471
Heparin, LMWH n (%)	65 (95.6%)	32 (100%)	33 (91.7%)	0.241
Dipyridamole, n (%)	18 (26.5%)	13 (40.6%)	5 (13.9%)	0.013 *
Steroid, n (%)	60 (88.2%)	31 (96.9%)	29 (80.6%)	0.058
Immune modulator, n (%)	8 (11.8%)	8 (25%)	0 (0%)	< 0.001 *
Antibiotics, n (%)	50 (73.5%)	28 (87.5%)	22 (61.1%)	0.014 *
Inotrope, n (%)	8 (11.8%)	8 (25%)	0 (0%)	0.001 *
ASA, n (%)	25 (36.8%)	19 (59.4%)	6 (16.7%)	< 0.001 *
P2Y12 inhibitor, n (%)	4 (5.9%)	2 (6.3%)	2 (5.6%)	1.00
Beta blocker, n (%)	15 (22.1%)	11 (34.4%)	4 (11.1%)	0.021 *
CCB, n (%)	12 (17.6%)	5 (15.6%)	7 (19.4%)	0.680
RAS blocker, n (%)	13 (19.1%)	6 (18.8%)	7 (19.4%)	0.942
Diuretic, n (%)	23 (33.8%)	20 (62.5%)	3 (8.3%)	< 0.001 *
Statin, n (%)	5 (7.4%)	4 (12.5%)	1 (2.8%)	0.180
Oxygen treatment via face mask, n (%)	33 (48.5%)	4 (12.5%)	29 (80.6%)	< 0.001 *
NIMV/HFNC, n (%)	22 (32.4%)	15 (46.9%)	7 (19.4%)	
Orotracheal intubation, n (%)	13 (19.1%)	13 (40.6%)	0 (0%)	
Adverse events during hospitalization				
Acute renal failure, n (%)	24 (36.4%)	16 (51.6%)	8 (22.9%)	0.015 *
Acute liver failure, n (%)	38 (57.6%)	18 (58.1%)	20 (57.1%)	0.940
Cerebrovascular accident, n (%)	3 (4.6%)	3 (9.7%)	0 (0%)	0.103
Myocardial injury, n (%)	31 (47.7%)	22 (73.3%)	9 (25.7%)	< 0.001 *
Hospital stay duration (days)	16 (2-55)	25 (7-51)	13 (2-55)	< 0.001 *

Abbreviations: BUN - blood urea nitrogen, CKD-EPI - estimated glomerular filtration rate, AST - aspartate transaminase, ALT - alanine transaminase, LDH - lactate dehydrogenase, CRP - C reactive protein, Hs-TnT - high-sensitivity troponin T, Pro-BNP - prohormone B-type natriuretic peptide, Hgb - hemoglobin, WBC - white blood cell, RBC - red blood cell, LMWH - low molecular weight heparin, ASA - acetyl salicylic acid, CCB - calcium channel blocker, RAS - renin angiotensin system, NIMV - non invasive mechanical ventilation, HFNC - high flow nasal cannula.