

The Association of Proteomic Biomarker(CCL3 & DOC2B) as Comparison between COVID-19 with DM & DM

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Abstract

Objective: assess the levels of both (CCL3 & DOC2B) of the disease to predict the frequency of acute cases and deaths associated with infection with the virus with the presence of diabetes.

Methods: the cross sectional study were (48), which were divided into 2 groups according as COVID-19 with DM (18) and DM (30).

Results: the current study shows there is significant difference in mean of CCL3 of diabetic was higher than CCL3 of covid-19 with diabetic and significant difference in the mean DOC2B of diabetic very higher than DOC2B of covid-19 with diabetic .

Conclusions: COVID-19 infection with diabetic patients leads to a decrease in the level of CCL3 and DOC2B Comparison with levels in DM

Introduction: Respiratory syndrome disease is characterized by severe acute respiratory syndrome symptoms. The elderly and those with serious illnesses (without taking into account the age of the patient) are exposed to increasing deaths (Christoforidis *et al.*, 2020). One of the main risk factors for pneumonia is the association of diabetes with it (Marhl *et al.*, 2020). On the other hand, the diabetes patients from the most vulnerable group when exposed Corona virus. There is association between diabetes and more severe injuries with corona virus (Huang *et al.*, 2020). Chemokine are a large family of chemo attractant cytokines for leukocytes and their receptors belong to a family of specific G-protein-coupled 7 trans membrane domain receptors. CCL3, also known as macrophage inflammatory protein-1 α (MIP-1 α), is a CC chemokine characterized as inducers of inflammatory process in various inflammatory autoimmune diseases. An intensive investigation done by Shehade *et al* disclosed that anti-CCL3 Antibodies were positive in nearly 87% of T1DM individuals, so anti-CCL3 Antibodies can be used as a powerful biomarker in T1DM (Zarch *et al.*, 2020).DOC2 family of proteins contains 3 isoforms: designated DOC2A, DOC2B, and DOC2C. DOC2B is a calcium sensor, which positively regulates SNARE (soluble N- ethyl maleimide sensitive factor attachment protein receptor) -dependent fusion of insulin vesicles with membranes in pancreatic beta cells . Double C2 domain β (DOC2B) is a calcium-sensitive protein that positively regulates the insulin-stimulated translocation of GLUT4 to the plasma membrane in adipocytes .In addition, DOC2B enhances insulin secretion in pancreatic beta cells (Zhang *et al.*,2020).

Serial No. Features Type1Type2

1	Frequency	10%-20%	80%-90%
2	Age of onset	Early, <35 y	Late, >40 y
3	Type of onset	Abrupt and severe	Gradual and insidious
4	Weight	Normal	Obese or nonobese
5	HLA	Linked to HLA DR3, HLA DR4, HLA DQ	No HLA association
6	Family history	<20%	Approximately 60%
7	Genetic locus	Unknown	Chromosomes 6
8	Diabetes in identical twins	50% concordance	80% concordance
9	Pathogenesis	Autoimmune destruction of β cells	
	Insulin resistance	impaired	

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insulin secretion

10 Islets of cell antibodies ~~Y~~No

11 Blood insulin level Decreased insulin Normal or increased

insulin

12 Islet-cell changes Insulin cell depletion No insulinitis, later brosis

13 Amyloidosis Infrequent Common in chronic cases

14 Clinical management Insulin, diet Diet, exercise, oral drugs, insulin

15 Acute complications Ketoacidosis Hyperosmolar coma

Methods: The cross sectional study conducted was completed in the laboratory unit of Clinical Biochemistry at Mirjan medical city in Babylon. The collection of samples was directed during the period from 1st of December 2020 until 30th of April 2021. the cross sectional study were (48), which were divided into 2 groups according as COVID-19 with DM (18) and DM (30).

Biostatistics analysis: In this study the data were calculated by Microsoft Excel 7 with the Statistical Package for the Social Sciences (SPSS) version 24. From IBM Descriptive statistic .it was expressed as mean with standard deviation (SD) for different among four group's patients. Mann-Whitney U and spearman analysis was used to evaluate the correlations between all variables. Significant differences were considered as $p < 0.05$ and more was non-significant. And used Receiver operating characteristics.

Results and Discussion: The mean Double C2-like domain (DOC2B) of diabetic (30.13) very higher than mean of Double C2-like domain (DOC2B) of covid-19 with diabetic (15.11) the difference was significant ($p < 0.05$).the previous study, where the effect of covid-19 was negative on diabetes patients this supported by (Zhang *et al.* , 2019) .These data are also consistent with previous findings that Double C2-like domain (DOC2B) positively regulates GLUT4 translocation in adipocytes, and that Doc2b-knockout mice have impaired insulin sensitivity and muscle glucose uptake.The mean of C-C motif chemokine ligand 3 (CCL3) of diabetic was (30.27) higher than mean C-C motif chemokine ligand 3 (CCL3) of covid-19 with diabetic (14.89). the difference was significant ($p < 0.05$).the previous study, where the effect of covid-19 was negative on diabetes patients this supported by that The association of individual C-C motif chemokine ligand 3 (CCL3) serum levels was seen in relatives with multiple islet autoantibodies, but not in islet autoantibody-negative relatives. There was a similar trend towards more cases of significant correlation between cytokines or chemokine in the relatives at high vs. moderate diabetes risk (7 vs. 2 cases) may be because of regional or genetic differences. (Moghaddom *et al.*, 2005).

Receiver operating characteristics (ROC): Receiver operating characteristics (ROC) curve analysis of CCL3 and DOC2B was performed. The best area under the ROC curve (AUC) was for CCL3 levels (AUC = 0.34) Asymptotic 95% Confidence Interval (0.217- 0.480) and for DOC2B levels (AUC=0.38) Asymptotic 95% Confidence Interval (0.268- 0.508) for COVID-19 with DM.

figure (1.1): Receiver operator characteristic curve analysis for the calculation of CCL3 &DOC2B for COVID-19 with DM.

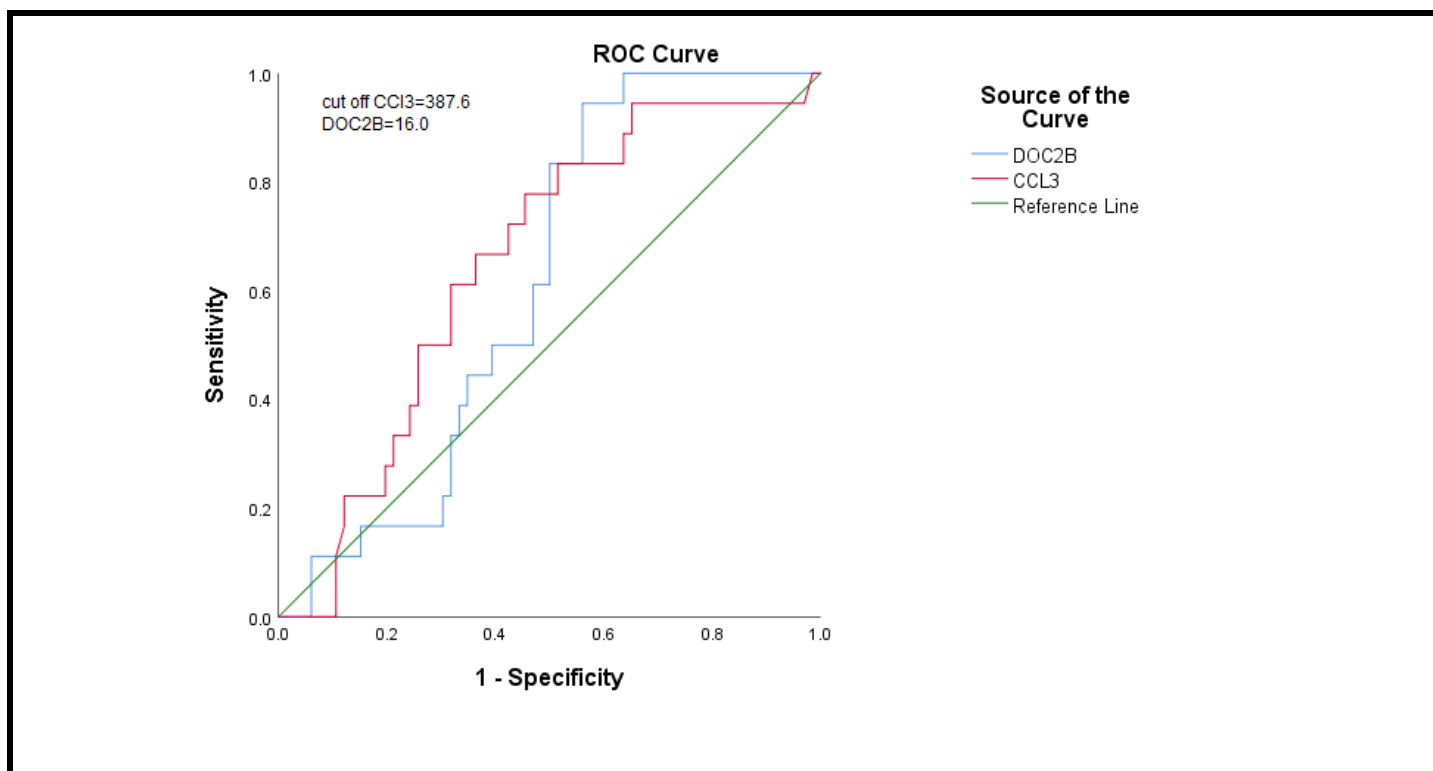


Table (1.1): Sensitivity and specificity of CCL3 &DOC2B for COVID-19 with DM.

Area Under the Curve					
Test Result Variable(s)	Area	Sensitivity	p value	specificity	Cut off
CCL3	.652	0.778	0.050	0.545	387.6
DOC2B	.612	0.833	0.147	0.500	16.0

Receiver operating characteristics (ROC): Receiver operating characteristics (ROC) curve analysis of CCL3 and DOC2B was performed. The best area under the ROC curve (AUC) was for CCL3 levels (AUC = 0.67), Asymptotic 95% Confidence Interval (0.662 - 0.876), cut off=424.3, sensitivity=0.767, specificity=0.759 and for DOC2B levels (AUC=0.61), Asymptotic 95% Confidence Interval (0.632- 0.872), cut off=16.0, sensitivity=0.800, specificity=0.78 for DM.

figure (1.2): Receiver operator characteristic curve analysis for the calculation of CCL3 &DOC2B for DM.

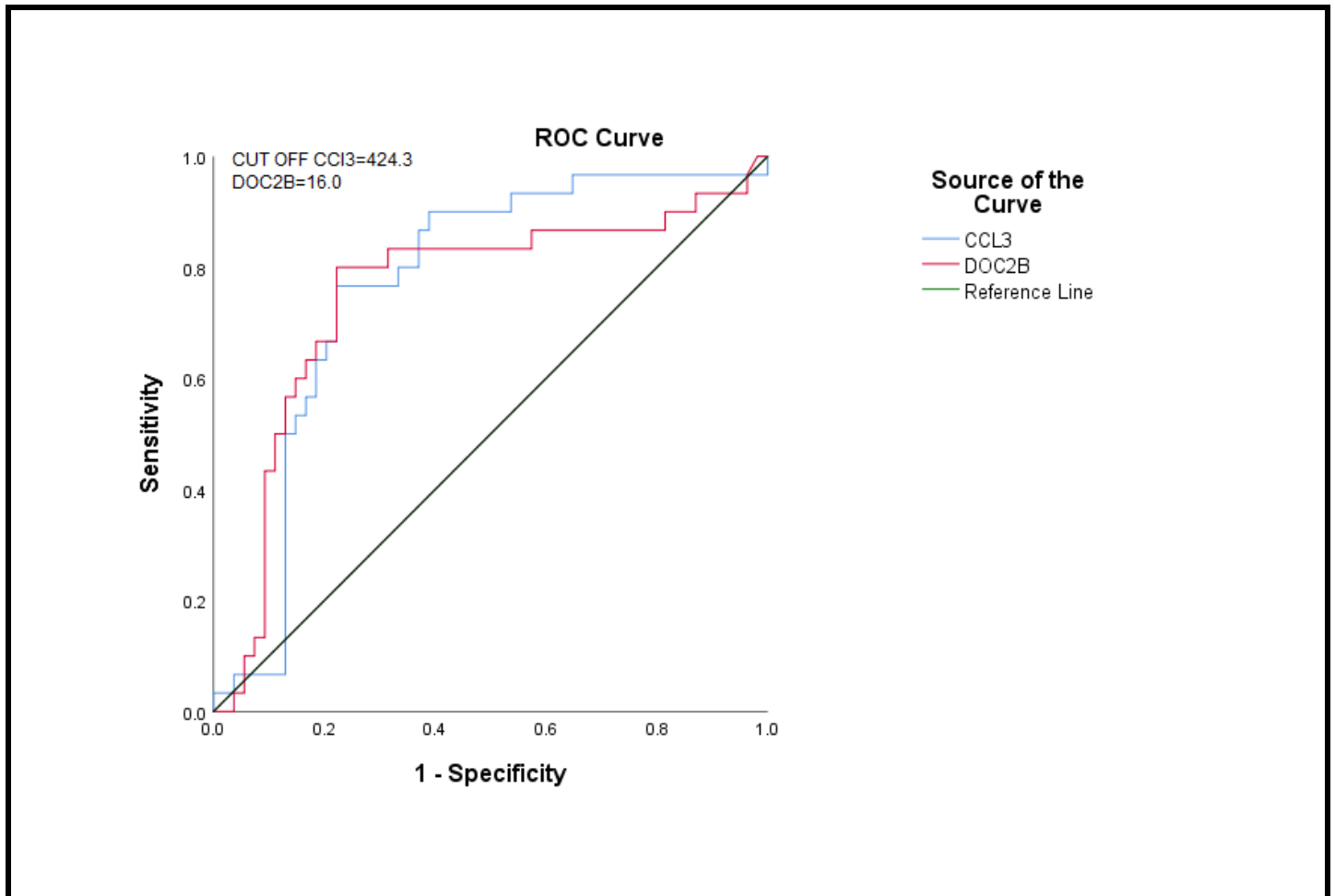


Table (1.2): Sensitivity and specificity of CCL3 &DOC2B for DM.

Area Under the Curve					
Test Result Variable(s)	Area	Sensitivity	p value	specificity	Cut off
CCL3	.769	0.767	.000*	0.759	424.34
DOC2B	.752	0.800	.000*	0.780	16.0

*Mann-Whitney U was significant $p < 0.05$

Conclusions: Both (CCI3 & DOC2B) are predictive factors for the risk of developing diabetes mellitus when infected with COVID-19, COVID-19 infection with diabetic patients leads to a decrease in the level of CCI3, COVID-19 with diabetic patients leads to a decrease in DOC2B,DOC2B and CCI3 are two markers that can be used as predictive to monitor diabetes with COVID-19.

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