Vap-1 as predictor severity of covid-19 patients

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Abstract

Introduction: Vascular adhesion protein-1 (VAP-1) is released by endothelial cells, adipocytes, and vascular smooth muscle cells that have functional monoamine oxidase activity. A copper-containing semi carbazide-sensitive amine oxidase (SSAO). The study's objective was to evaluate the VAP-1 level in patients with COVID-19. The 81 KDa sialo glycoprotein known as vascular cell adhesion molecule 1 (VCAM-1) is expressed by dendritic, macrophage-like, and cytokine-activated vascular endothelium cells. It belongs to the superfamily of immunoglobulins.

Material and method: The hospital central laboratory used the normal laboratory procedure to examine the serum and complete blood count. We used commercially available assays to evaluate VAP-1..

Results: Patients with mild COVID-19 had median blood levels of VAP-1 that were considerably greater than those with severe disease (3687.00 (1654.50) pg/ml versus 3664.00 (1055.50) pg/ml, respectively; P = 0.009). Conversely, patients with severe COVID-19 had median blood levels of VCAM-1 that were considerably greater than those with mild illness, measuring 271.31 (255.95) pg/ml against 198.30 (105.05) pg/ml, respectively (P = 0.004).

Conclusions: Vascular adhesion protein-1 (VAP-1) is more specific and sensitive than VCAM-1for COVID-19.

Keywords: COVID-19, levels vascular adhesion protein-1 (VAP-1), D-dimer, coagulopathy, ferritin.

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Introduction

The extremely contagious coronavirus illness is caused by the infectious pathogen (COVID-19) [1]. After being initially discovered in Wuhan, China, the COVID-19 virus swiftly spread and became an unparalleled worldwide pandemic. Not only does the new coronavirus impact the respiratory system, but it also impacts other parts of the human body. [2].

COVID-19 may cause damage to the heart, lungs, liver, kidney, arteries, and other organs. [3]. Most inpatient COVID-19 patients suffer from catastrophic multi-organ failure, significant lung injury, and hemolytic anemia. Acute respiratory distress syndrome (ARDS) and respiratory failure are the most common consequences of a severe COVID-19 infection. Shock, hypoxic encephalopathy, acute liver, kidney, and heart infections, and super infection are less common symptoms. Furthermore, tissue damage symptoms such hemoptysis or rhabdomyolysis, which result in cellular death and the release of hem proteins, may be present in certain COVID-19 patients. [4].

The abnormal production and deregulation of numerous inflammatory cytokines are hallmarks of a systemic inflammatory response triggered by COVID-19 [5]. The expression of several inflammatory factors, such as cytokines like interleukin (IL)-1, IL-6, and IL-18, chemokines like fractalkine (FKN), and adhesion molecules like intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1), is largely responsible for the recruitment and activation of immune cells. [6]. Numerous investigations have emphasised pathogenic symptoms in patients infected with COVID-19, such as widespread endothelial inflammation, direct viral infection of endothelial cells, and venous thromboembolism [7]. As a result, assessing the expression and control of endothelial adhesion molecules in COVID-19 is crucial for both clinical and research purposes since it could reveal information about the pathogenesis of the illness and possible targets for treatment. [8].

One of the endothelial cell adhesion molecules that facilitates lymphocyte attachment to the endothelium under shear stress is vascular adhesion protein 1 (VAP-1). [9]. VAP-1 is mostly expressed in the endothelium of lymph nodes and hepatic endothelia under normal circumstances, but it is also induced in the arteries of many tissues, including the tonsil, stomach, skin, and synovia, when chronic inflammation is present. [10] Because it may facilitate shear-dependent adherence to hepatic sinusoids, a vascular bed in which selectins seem to play a minor role, VAP-1 seems to have a specific purpose in the liver. The majority of research indicates that selectins, the most prevalent tethering receptor, are not expressed at all on the hepatic sinusoids, and functional investigations conducted on animals with specific deficiencies indicate that selectins play a negligible role in the hepatic sinusoids. [11]. Therefore, VAP-1's capacity to facilitate lymphocyte tethering to the liver endothelium implies that it will be essential for controlling lymphocyte homing to the liver. [12]. Inflammatory cytokines like TNF-α and IL-1β, as well as the activation of toll-like receptors on endothelial cells, fibroblasts, and dendritic cells, are some of the variables that affect VCAM-1 expression. Furthermore, TNF-α and reactive oxygen species (ROS) can activate the NF-κB transcription factor, which controls the transcription

of the VCAM-1 gene. Soluble VCAM-1 levels in the blood have been connected to a number of cardiovascular disease processes, such as post-operative atrial fibrillation. [13], but are also seen to rise as soon as three hours following a standard cardiopulmonary bypass. [14].

Materials and Method

Serum samples were collected and stored at -70°C before to analysis. All of the diagnoses were made using standard clinical, biochemical, and histologic criteria. There were 19 samples with severe COVID-19 and 69 samples with mild COVID-19 among the patients.

Each concentration of the solution was replicated and added to one well side by side (100 uL per well) after the standard working solution was added to the first two columns. After adding the samples to the remaining wells (100 uL each), the plate was sealed using the kit's sealer and incubated at 37°C for 90 minutes. 100 µL of the Biotinylated Detection Ab working solution was added to each well after the liquid had been removed. The plate sealer was coated with mix-up incubation for an hour at 37°C. Each well received 350 uL of wash buffer after the solution was aspirated from it. Drain the solution from each well after soaking for one to two minutes, then use fresh absorbent paper to pat dry. Repeat this washing procedure three times. After adding 100 µL of HRP Conjugate working solution to each well, the plate sealer was applied, and the mixture was incubated at 37°C for 30 minutes.

As in step 3, each well's solution was aspirated, and the washing process was carried out five times. After adding 90 µL of the substrate reagent to each well, it was sealed with a new plate sealer and incubated for around 15 minutes at 37°C. 50 µL of a Stop Solution was added to each well. Using a microplate reader set to 450 nm, the optical density (OD value) of every well was measured simultaneously.

Result

88 hospitalized individuals with confirmed COVID-19 were included in the research. Patients with varying degrees of sickness were divided into two groups. The table displays the fundamental characteristics of mild [n = 69] and severe [n = 19] patients. Mild patients had a significantly higher biomarker (Vap-1) median [3687.00] than sever patients [2089.00 to 9130.00] and severe patients [23664.00 to 4756.00] median [3664.00]. The most common symptoms at the start of the illness were fever, coughing, tiredness, expectoration, and dyspnea. Headache, nausea, vomiting, muscular pains, diarrhea, and chest discomfort were among the other symptoms. More over half of the patients had chronic conditions.

Tabel1. Show median (Range) between mild and sever

	Mild Cases– severe Case comparison		
Vap-1 (pg/ml)	***mild covid-19 patients* N=69**	***severe covid-19 patients* n=19**	***P***
Range	2089.0– 9130.0	2347.0– 4756.0	**0.009 † S**
Median	3687.0	3664.0	

A white blood cell comparison between patients with severe and mild COVID-19 was conducted, and the results are shown in table (2). The mean WBC levels of patients with severe COVID-19 were greater than those of patients with mild COVID-19, at 19.07 ± 3.8 versus 14.89 ± 3.0. The mean lymphocyte count of severe COVID-19 individuals was 4.2 ± 3.0, which was lower than the mild value of 6.27 ± 3.4. The difference, however, was noteworthy (P = 0.031). Additionally, D-dimer severe patients' mean was higher at 913.31 ± 262.1 than that of mild patients (815.12 ± 209.5). However, the difference was not statistically significant (P = 0.759).

Table 2. Show median among D-dimer, lymphocyte and WBC

	Mild Cases– severe Case comparison		
	***mild covid-19 patients* N=69**	***severe covid-19 patients* n=19**	***P***
White blood cells			
Mean± SD	**14.8** ± 3.0	**19.07** ± 3.8	**0.001 † HS**
Range	10.4 – 26.2	12.6 – 24.8	
SE	**0.37**	**0.94**	
Lymphocyte			
Mean± SD	**6.27** ± 3.4	**4.2 ±** 3.0	**0.031 † S**
Range	1.6 - 17.2	1.2 - 11.2	
SE	**0.41**	**0.73**	
D-dimer			
Mean± SD	**913.31** ± 262.1	**815.12** ± 209.5	**0.759 † NS**
Range	101.0 - 7622.0	367.7 - 3483.0	
SE	**151.9**	**172.0**	

A study of blood VCM-1 levels between severe and mild COVID-19 patients was conducted, and the findings are shown in table (3-14). Serum Vcm-1 median levels in severe COVID-19 patients were significantly greater than those in mild COVID-19 patients, ranging from 271.3 (255.9) pg/ml to 198.3 (105.0) pg/ml (P = 0.004).

Tabel 3. Show median (IQR) between mild and sever

	Cases of COVID-19		
VCM-1 (pg/ml)	***mild covid-19 patients*** **N=69**	***severe covid-19 patients*** **N=19**	***P***
Range	34.6– 562.4	98.2 – 467.6	**0.004 ŧ**
Median	198.3	271.3	**S**

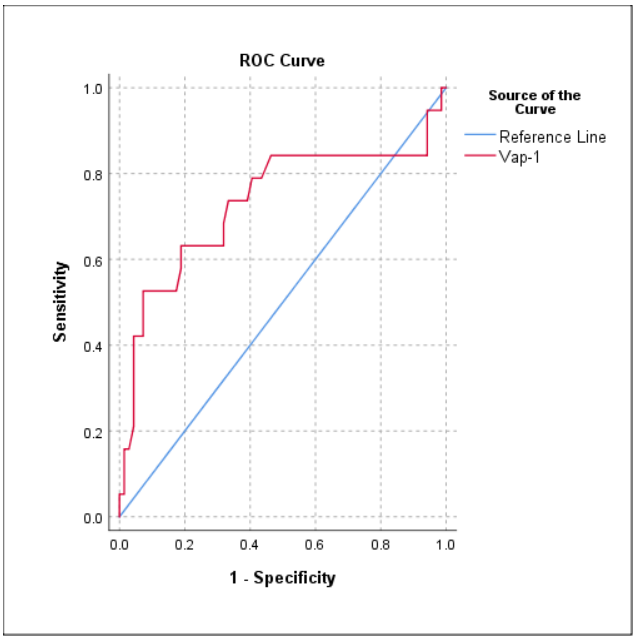

Figure1. Sensitivity and specificity of vap-1

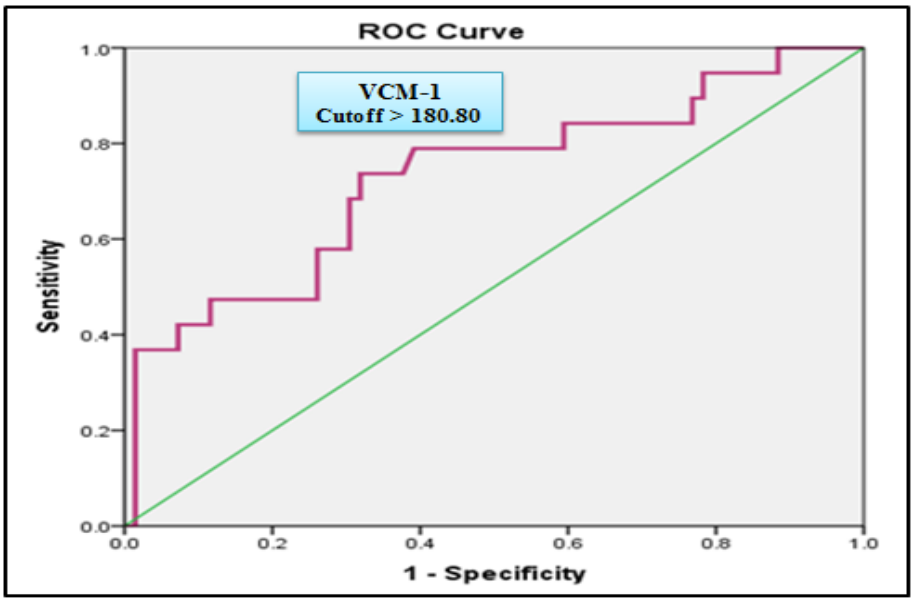

Figure 2. Sensitivity and specificity of vcam-1

Discussion

The COVID-19 pandemic started in December 2019, swiftly expanded over the world, and is currently a serious public health concern. In this study, we present eighty-eight patients who had laboratory-confirmed SARSCoV-2 infection. [15]. Frequently lead to lower respiratory tract disease, and disease severity was influenced by initial viral titers in airways, age and comorbid conditions.[16].

72.3% (99/137) of the patients exhibited a form of lymphocytopenia, while nearly 80% of the patients had either normal or decreased white blood cell counts. [17]. Furthermore, nine individuals had PCT findings that were all negative and peripheral white blood cell counts that were almost normal. Lymphopenia was linked to MERS and SARS infections. [18]. Similarly, COVID-19 patients often experienced lymphopenia, which was especially apparent in patients in the critical care unit. [19]. More cells experienced apoptosis following excessive inflammatory responses, according to studies of SARS infection, and the mechanisms behind lymphopenia in SARS-CoV-2 infection may be connected to reduction of cellular immune effective function. The results of the lymphocytes may have an impact on the disease's severity and death. Due to large inflammatory cell infiltration and cytokine storms, both MERS and SARS infections—which have been notably emphasized for the pathophysiology of hCoV infections—may result in severe lung damage and the syndrome of acute respiratory distress. [20].

Patients with severe COVID-19 had significantly higher D-dimer levels, and the meta-analysis verified that D-dimer levels more than 0.5 μg/ml were linked to a higher risk of severe COVID-19.30-D-dimer tests are commonly used in clinical practice to rule out the diagnosis of

deep vein thrombosis or pneumonia. A higher risk of abnormal blood clotting is indicated by elevated D-dimer. Greater D-dimer levels were also linked to a greater risk of death from community-acquired pneumonia. [21]. D-dimer levels within the normal range indicated a lower risk of sequelae, but dimer levels were considerably higher in patients with severe community-acquired pneumonia. [22]. Increased urokinase activity may produce hyperfibrinolysis in a mouse model of SARS-CoV illness by speeding up the cleavage of plasminogen into active plasmin, which eventually results in widespread alveolar damage and acute injury to the lungs. Our cohort analysis revealed elevated levels of coagulation function indicators, including pro-thrombin time, fibrinogen, fibrin degradation products, and D-dimer, in patients with severe COVID-19. Presumably, the severity of COVID-19 may also be associated with coagulation failure [23].

Increased levels of endothelial cell adhesion molecules are related to COVID-19 and the severity of the illness, and it may be a role in coagulation dysfunction. Given that blood vessels are the primary site of VAP1 expression, the vascular bed is most likely the primary source of sVAP-1. [24] VAP-1 is constitutively expressed in the human liver, and immunohistochemistry shows substantial staining in both normal and inflamed livers. However, VAP-1 expression and turnover are expected to be increased in the hepatic vascular bed in chronic inflammatory disease due to its critical role in controlling lymphocyte binding In the presence of persistent inflammation, VAP-1 transcription is up-regulated at several locations. A few patients gave us peripheral venous, hepatic, and portal blood [25].

Patients with severe COVID-19 had higher median serum Vcm-1 levels than those with mild COVID-19. Numerous infections, including those caused by the SARS virus family, are associated with endothelial dysfunction, which is characterized by reduced nitric oxide (NO) production and increased release of inflammatory markers such VCAM-1. The distinct affinity of the viruses for the angiotensin-converting enzyme-2 (ACE2) receptor, which is expressed in vascular endothelial cells, suggests that COVID-19 has a direct impact on the vascular endothelium. In conditions like hypertension, diabetes, coronary heart disease (CHD), and kidney failure, which have all been shown to be significantly correlated with the severity of COVID-19, reduced nitric oxide bioavailability, a sign of endothelial dysfunction, is believed to occur early. [26].

Conclusion

In summary, Vap-1 levels showed a significant difference between mild and severe COVID-19 cases ($P = 0.009$), indicating a possible role in disease progression.VCM-1 levels were substantially higher in severe cases ($P = 0.004$), reflecting strong association with increased disease severity. Both Vap-1 and VCM-1 may serve as useful biomarkers for evaluating COVID-19 severity and supporting clinical risk stratification.

Recommendation

Vap-1 and VCM-1 are promising supportive biomarkers that may help distinguish between mild and severe cases of COVID-19. To confirm their clinical value, larger and multi-center studies are needed to ensure reliability and broader applicability. Additionally, combining Vap-1 and VCM-1 with other inflammatory markers may enhance the accuracy of severity prediction and support early clinical decision-making.

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