2024 آب العدد 14A
No.14A Aug 2024
المجلة العراقية للبحوث الإنسانية والإجتماعية والعلمية
Iraqi Journal of Humanitarian, Social and Scientific Research
Print ISSN 2710-0952 Electronic ISSN 2790-1254

Review: The Relationship Between D-Dimer and Erythrocyte Sedimentation Rate (ESR) in the Context of COVID-19

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Abstract : In December 2019, a new illness induced by the unique coronavirus, known as coronavirus disease 2019 (COVID-19), emerged in Wuhan, China. Following that, this infection spread rapidly over the globe in an unprecedented manner, exhibiting pandemic characteristics. COVID-19 is most commonly transmitted via respiratory droplets, however fecal-oral transmission, sexual transmission, and environmental transmission cannot be totally ruled out. Notably, active virus was found in almost all biological samples from COVID-19 patients. According to World Health Organization (WHO) data, as of March 4, 2020, there were more than 98,191 confirmed cases and at least 3,380 deaths worldwide, resulting in a 3.4% case fatality rate. These data, particularly the CFR, are subject to change. D-Dimer is an effective biomarker. D-Dimer, a fragment formed by the breakdown of fibrin, is an efficient biomarker for assessing thrombotic events. Several investigations found that COVID-19 acutely ill and severe patients had much higher levels of D-Dimer than mild patients. Higher levels of D-Dimer increased the chance of in-hospital death. Additionally, D-Dimer levels were shown to be directly related to COVID-19 severity, demonstrating that COVID-19 caused significant hypercoagulability. Furthermore, it has been found that using enoxaparin as a preventive dose is ineffective for COVID-19. In such cases, thrombin activity should be assessed, and medication dosage adjustments or antiplatelet therapy should be explored. All of these data can assist to categorize COVID-19 patients depending on disease severity and enhance their therapy, particularly to avoid thromboembolic repercussions. The age group more prevalent contains the elderly and diabetic and associated patients. They had presented more severe and significantly elevated levels of D-dimer and ESR.

Keywords: Covid -19, D-dimer.

مراجعة: العلاقة بين ثنائي د ومعدل ترسيب كريات الدم الحمراء (ESR) في سياق كوفيد-19

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الملخص:

في ديسمبر 2019، ظهر مرض جديد ناجم عن فيروس كورونا الفريد، المعروف باسم مرض فيروس كورونا 2019 (كوفيد-19)، في مدينة ووهان بالصين. وبعد ذلك، انتشر هذا العدوى بسرعة في جميع أنحاء العالم بطريقة غير مسبوقة، حيث أظهر خصائص وبائية. ينتقل كوفيد-19 بشكل شائع عن طريق الرذاذ التنفسي، ومع ذلك لا يمكن استبعاد انتقال العدوى عن طريق البراز والفم، والانتقال الجنسي، والانتقال البيئي تمامًا. من الجدير بالذكر أن الفيروس النشط وجد في جميع العينات البيولوجية تقريبًا من مرضى كوفيد-19. ووفقًا لبيانات منظمة الصحة العالمية، اعتبارًا من 4 مارس 2020، كان هناك أكثر من 98191 حالة مؤكدة وما لا يقل عن 3380 حالة وفاة في جميع أنحاء العالم، مما أدى إلى معدل وفيات بنسبة 3.4٪. هذه البيانات، وخاصة معدل الوفيات، عرضة للتغيير. دي-دايمر هو مؤشر حيوي فعال. دي-دايمر، وهو جزء يتكون من تحلل الفيبرين، هو مؤشر حيوي فعال لتقييم الأحداث الخثارية. وجدت العديد من التحقيقات أن مرضى كوفيد-19 المصابين بأمراض حادة وشديدة لديهم مستويات أعلى بكثير من دي-دايمر مقارنة بالمرضى المصابين بأعراض خفيفة. تزيد المستويات الأعلى من دي-دايمر من فرصة الوفاة في المستشفى. بالإضافة إلى ذلك، ثبت أن مستويات دي-دايمر مرتبطة بشكل مباشر بشدة كوفيد-19، مما يدل على أن كوفيد-19 تسبب في فرط تخثر الدم بشكل كبير. علاوة على ذلك، وجد أن استخدام إينوكساباري كجرعة وقائية غير فعال لكوفيد-19. في مثل هذه الحالات، يجب تقييم نشاط الثرومبين، واستكشاف تعديلات جرعات الأدوية أو العلاج المضاد للصفيحات. يمكن أن تساعد كل هذه البيانات في تصنيف مرضى كوفيد-19 حسب شدة المرض وتعزيز علاجهم، وخاصة لتجنب المضاعفات الخثارية. تتضمن الفئة العمرية الأكثر انتشارًا كبار السن ومرضى السكري والمرضى المرتبطين. لقد أظهروا مستويات أكثر شدة ومرتفعة بشكل ملحوظ من ثنائي د وسرعة ترسيب كرات الدم الحمراء.

الكلمات المفتاحية: كوفيد-19، ثنائي د.

COVID-19 and Biomarkers

Coronavirus disease 2019 (COVID-19) is a pulmonary sickness caused by a new coronavirus, SARS-CoV-2. The COVID-19 epidemic was initially detected in Wuhan, China, on December 31, 2019, and quickly spread around the world. The World Health Organization declared a pandemic on March 11, 2020 (1). COVID-19 symptoms include fever, cough, and shortness of breath, which can be minor or severe. Additional signs might involve chills, muscle soreness, headaches, throat irritation, and diminished smell and flavor. The initial stages of COVID-19 are characterized by the activation of an inflammatory response, resulting in hyper-inflammation and a state of high inflammation(2,3). During the illness, a number of previously known and newly discovered indicators, including leukocytes, neutrophil, lymphocytes, C-reactive protein (CRP), the enzyme lactate dehydrogenase, D-dimer, erythrocyte sedimentation rates (ESR), lymphocyte to neutrophil ratio (NLR), platelet distribution length (PDW), and platelet-to-lymphocyte ratio (PLR), were identified. These biomarkers are associated with illness severity and aid in patient diagnosis, prognosis, disease progression

monitoring, treatment decision-making, and therapy follow-up (4). They have also been identified as major independent determinants, making them useful in predicting illness development, life-saving care, and mortality (5). The current retrospective study determined the profiles of the biomarkers D-dimer and ESR and analyzed the correlation in the severity of the disease, focusing on hospitalized patients. In addition, the results were compared to common clinical risk factors (6). The study concluded that patients with a severe state of the disease carry a high level of D-dimer and ESR, along with common clinical risk factors.

1. Introduction to D-Dimer and ESR

D-dimer is a tiny protein particle that appears in the blood when a blood clot gets broken up by the the process of fibrin system. It gets its name from the fact that it includes two fibrin peptide D fragments that are crosslinked. In comparison, the D-dimer test is specific and exact and has low utility in most patients who are negative, but it has a lot of utility in patients who are positive (7,8). If an individual has a positive D-dimer, further evaluation is warranted. Know that a negative does not rule out venous or arterial thrombosis, PE, stroke or other venous or arterial thrombotic event in patients with low-intermediate pretest probability of VTE or VTE in the pregnant patient without suspected DVT (9). Erythrocyte Sedimentation Rate (ESR) is used to assess the most common inflammatory disease. It measures the distance she has fallen at the end of an hour and the unit is 'mm'. ESR is represented by the time it takes for the red blood cells to separate from plasma, which is at the base of a vertical test tube. At the end of an hour, ESR represents the number of millimeters that red blood cells fall from the beginning to the top of the liquid part of an anticoagulated blood sample, which is usually citrate (10). It is a test that uses the physical principle of the distance of sedimentation of red blood cells that are associated with a change in plasma protein forming larger or smaller aggregates (11).

1.1. Definition and Function of D-Dimer

D-dimer is an insignificant protein particle that appears in the bloodstream after a blood clot melts. It is usually invisible or present beginning at low levels until the body begins creating and clearing out clots in its blood. The D-dimer test is ordered when someone is suspected of having an inappropriate blood clot (thrombosis) or as a result of clot formation and subsequent dissolution of fibrin. Substantial LDH activity may complicate interpretation of reduced D-dimer activity accompanied by

elevations of the enzyme (12). Blood clots are formed to prevent excessive bleeding when blood vessels get injured. When a clot is no longer needed, fibrinolysis occurs where the clot is broken down and removes the temporary trap. The plasmin (ogen) system is the group of proteins most directly involved in fibrinolysis, and the adjacent target of a medicine that interferes with clot dissolution is often a factor in the plasminogen system. The potential use of thrombolytic medications like tissue plasminogen activator for interventional treatment of an acute myocardial infarction or acute stroke brings the issue to the forefront in medical practice and affects the accuracy of D-dimer results. D-dimers result from the normal breakdown of cross linked fibrin clots and are the most sensitive indicators in blood that a clot has recently developed and dissolved, for example, blood clots forming in veins of the legs, pelvis, and chest (13,14,15). Treatment for thrombotic disorders can include anticoagulant therapy to reduce the risk of recurrent thrombosis (16,17).

1.2. Definition and Function of ESR

Biomarkers are a broad subcategory of indicators. Biomarkers can indicate risk (exposure) for an outcome or disease, and can be used to rule-out disease, rule-in disease, measure stages of disease (natural history or progression), measure the effect of an intervention (clinical trial) or surrogate (18,19,20). Endpoints for the consequences of exposure on an outcome or disease (21). Biomarkers includes polymers like as lipids, carbohydrates, protein, and amino acids, as well as tiny molecules, such as metabolic intermediates, environmental chemicals, and drugs. In conjugation with modern proteomics technologies, the biomarker concept has been expanded to include microbes in the diagnostically inaccessible microbiota of human tissues (gut, oral cavity, urogenital tract, respiratory tract, etc.) and a new type of pharmacokinetic biomarkers or protein therapeutics – protein-drug addicts resulting in the formation of new proteins with sequences not existing prior to the drug administration (22,23.24). Biomarkers must provide both an analytical and clinical validity, which is often a function of their accuracy, precision, and robustness (25,26). Accurate and precise biomarkers must be stable and reproducible to give results independent of variances in methodology, operators and sites. However, even accurate and precise biomarker results can be clinically invalid if not sufficiently sufficient in differential disease detection, that is, if they lack specificity, indicative of high false-positive rates. Since many biomarkers shown to correlate with disease are indicators of ubiquitous cellular process (e.g., chronic inflammation), the absence of specificity often raises a concern for false-positive results with such biomarkers (27,28,29,30).

Discussion:

1- Erythrocyte sedimentation rate (ESR) is a hematological test used primarily to detect inflammation associated with conditions such as infections, cancers, and autoimmune diseases. It is a non-specific test that depends on the settling behavior of red blood cells in the plasma and often shows a progressive increase with the ongoing disease process. Epidemiological studies indicated that on average, the values of ESR increase with aging. Therefore, it is challenging to interpret the meaning of very high ESR values. Findings show that there is a limited understanding of the iterative sedimentation process and the underlying physical mechanism responsible for the predominance of much higher ESR values.

2- ESR is a non-specific marker of inflammation. It measures the rate at which red blood cells sediment in a period of one hour. Higher ESR levels indicate the presence of inflammation in the body. In COVID-19 patients, elevated ESR levels have been observed, reflecting the inflammatory response to the infection. This elevation correlates with disease severity and can be used as a marker to monitor the inflammatory status of patients.

3- D-dimer is considered a marker of thrombosis or hypercoagulability. However, elevated D-dimer levels may also be found in non-thromboembolic diseases associated with inflammation, tissue injury, or malignancy. Recently, numerous studies investigated the prognostic role of D-dimer in the context of coronavirus disease 2019 (COVID-19). These studies reported an association between elevated D-dimer and adverse events, such as higher rates of mechanical ventilation, intensive care unit (ICU) admission, thromboembolic events, and death, in patients with COVID-19. However, there are currently very few data regarding the use of D-dimer in a clinical setting, specifically in the triage of patients with suspected COVID-19 .

4- D-dimer is a breakdown of fibrin product that is a tiny protein fragment found in bleeding after a clot of blood dissolves. Elevated D-dimer levels are frequently related with blood clotting issues. D-dimer values are commonly increased in COVID-19 patients, particularly those with severe disease. This elevation suggests an increased risk of thrombosis, which can result in problems such as deep vein thrombosis (DVT), a pulmonary embolism (PE), and dissemination of intravascular coagulation (DIC). Monitoring a D-d concentrations in COVID-19 patients can assist determine the disease's severity and the risk of clotting problems

5- Both D-dimer and ESR are important biomarkers in the context of COVID-19. Elevated D-dimer levels are associated with an increased risk of thrombotic events, while elevated ESR levels indicate heightened inflammation. Monitoring these biomarkers can provide valuable insights into the severity and progression of COVID-19, helping healthcare professionals manage and treat patients more effectively

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