The Effect of Bacterial Infections on Some Hematological Parameters in Patients with Leukemia

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Abstract

Objective: Our research aims to evaluate correlation between D-Dimer, Platelets (PLT), Prothrombin time (PT) and bacterial infection in patients with acute leukemia.

Method: The research took place between October 2021 and May 2022. Karbala Health Directorate / Imam Hussein Center for Oncology and Hematology. A venous blood sample of 10 mL was obtained from 104 acute leukemia patients and 50 healthy volunteers. We must follow critical blood culturing procedures, following which Hematological parameters must be determined (D-Dimer, PLT and PT).

Results: 104 new acute leukemia (AL) cases, A total of 62 patients (59.62%) were males and 42 patients (40.38%) were females, with 48 (46.15%) diagnosed with acute lymphoblastic leukemia (ALL) and 56 (53.85%) diagnosed with acute myeloid leukemia (AML), 16 with bacterial infection and 88 without bacterial infection. 50 healthy persons, 28 persons (56%) were male and 22 persons (44%) female, the results of D-Dimer(1586.492) ng/ml, PLT(132.826) µl,, PT(14.801) sec.

Conclusions: the study were presented association between of high level of D-Dimer and bacterial infections in leukemia patients, while PT and PLT level were not related with infection, but related with disease

Keywords: WBC, IL-6, CRP, Acute Leukemia, bacterial infection, AML, ALL.

1. Introduction

Acute leukemia is a kind of blood cancer in which immature progenitor cells in the bone marrow clonally grow. If left untreated, this infiltration leads to severe thrombocytopenia, anemia, and leukopenia, which can lead to death in a matter of weeks [1]. Depending on the blast cell's origin, acute leukemia can be divided into two types:

Acute meroblastic leukemia (AML)

Acute lymphoblastic leukemia (ALL) [2].

Acute myeloid leukemia (AML) is a type of leukemia that affects the bone marrow. Clonal proliferation and differentiation arrest of myeloid progenitor cells are characteristics of AML. which lose their ability to differentiate and respond to regular proliferation regulators In the absence of treatment, this loss results in deadly infection, hemorrhage, or organ invasion within a year of diagnosis [3]. The annual incidence of AML in the United States (US) is 4.3 per 100,000 people, adjusted for age. In the United States, the occurrence rises with age; AML has a variety of causes, and the median age at diagnosis is 68 years [4]. (ALL) is a leukemia that causes more than 30% lymphoblasts to form in the bone marrow or blood [5]. ALL can affect adults and children, however it is most frequent in children aged 2 to 5. A variety of factors are known to contribute to ALL, including external and endogenous exposures, genetic predisposition, and chance [6]. In acute leukemias, particularly acute myeloblastic leukemia (AML), bleeding symptoms are common and apparent in the early stages of the disease. Hemostatic diseases involving the consumption of coagulation factors and platelets, as well as thrombocytopenia caused by blast cell invasion of the bone marrow, are common causes of these symptoms. Thrombosis of the major arteries is uncommon in AML, although it is becoming more common in both children and adults with acute lymphoblastic leukemia (ALL) [7]. Coagulation problems, particularly due to DIC, are common at the time of diagnosis in acute leukemias, and are more common in AML than ALL. All leukemia patients, especially those diagnosed with AML, should have routine DIC screening done at the time of presentation [8]. DIC is determined by examining coagulation markers such as D-dimer levels, prothrombin time, thrombin time, fibrinogen concentration, and platelet counts [9].

A positive blood culture isolation linked to clinical signs was characterized as a bloodstream infection (BSI). BSI is a potentially fatal life-threatening a complication of a hematologic cancer. To provide a direct basis for blood infections, blood cultures and medication sensitivity testing were performed [10]. In the United States, sepsis is among the top ten causes of death. The mortality rate of individuals with sepsis is reduced by several fold when infections are delayed in starting or being covered [11]. Patients with hematological malignancies who receive chemotherapy or hematopoietic stem cell transplantation are at a high risk of infection. In people with hematological cancers, the common symptom of fever makes it more difficult to distinguish infectious from noninfectious episodes. Microbial infection, graft-versus-

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host disease, engraftment syndrome, and thrombotic microangiopathy are just a few examples of what can cause a fever; as a result, recognizing the source of the fever is critical for appropriate antibiotic therapy [12]. Gram-negative bacteria were the most common pathogens in acute leukemia patients [13, 14]. D-D is useful indicators for determining the severity of an illness [12].

Materials and Methods

A case-control study of individuals with acute leukemia was carried out from October 2021 to May 2022. In the Imam Hussein Center for Oncology and Hematology / Karbala Health Directorate, One hundred four patients were diagnosed with acute leukemia. All of the patients were adults, between the ages of eighteen and eighty, of both sexes, who were diagnosed with acute leukemia. A total of 10 milliliters of blood flowed through the veins of acute leukemia patients were collected. Nutusi et al. performed an important blood culturing process that should be followed [14].

The The patient's identification had been established and the the patient's name had been questioned. To double-check identification,Look at the patient's paperwork or the wall over the bed.

The patient was informed about the procedure as well as the specifics of the plans, Verbal approval was frequently gained.

Blood culture bottles, sterile gloves, tourniquet, adhesive strip, povidone iodine or alcohol solution (or other appropriate skin disinfection), and sterile pack of cotton/gauze swabs were all collected.

A tourniquet was applied, and a suitable vein was selected. Hands were cleaned with soap and water or disinfected with alcohol. After that, the hands were cleaned or rubbed until fully dry. The gloves were put on with sterility in mind.

Povidone or an alcohol solution was used to clean the puncture site in an aseptic approach. For 1 to 2 minutes, the disinfectant was allowed to dry. A green sterile cover with an aperture was used to cover the blood culture site. The patient's blood vessel was punctured with a needle, yielding at least 10 milliliters of blood (adults). If the vacutainer was utilized, the blood culture would be taken first.

The tourniquet was removed. The syringe and needle were extracted from the wound of penetration. The puncture site was cleaned with a dry swab before pressure was applied. Inoculate blood into culture bottle after cleaning the lid of the blood culture container with an alcohol swab if blood was not drawn directly into the culture bottle using the vacutainer method. Before collecting blood for additional testing, vaccinate the blood culture tube. There is a lot to accomplish between taking blood and inoculating the blood culture vial.

a jar for blood cultures was gently turned to mix the blood and culture material (Avoided shake vigorously).

The blood culture vial was delivered to the laboratory as quickly as possible. At the same time, 2 mL of blood was deposited at room temperature in a gel tube (2 mL) and allowed to coagulate for at least fifteen minutes before centrifugation at 2500 rpm. The serum was then split into epindrops. The leftover blood sample (1.5ml) was placed in an Ethylenediaminetetraacetic acid (EDTA) tube and shaken for at least fifteen minutes.

All specimens went through culture and sensitivity tests, blood was drawn from a vein in the arm and placed in blood culture flasks. For the first time, The blood cultures were evaluated using the BacT/ ALERT® 3D system (bioMeriéux, Marcy l'Etoile, France). Before being incubated at 35°C in a 5% CO2 atmosphere, the bacteria were collected and put on blood agar plates (BAP; Asan Pharmaceutical Co., Ltd., Seoul, Korea) and MacConkey agar plates (Becton Dickinson, Sparks, MD, USA). And analysis to Hematological tests, were In the human clot junior device, PT was measured manually on semi-automates BIO SOLEA 2, BIO SOLEA 4. swelab to evaluate CBC was followed by Cielińska et al. [15],and D-Dimer was measured automatically in the VIDAS® D-Dimer Exclusion II™ (DEX2) followed by Goebel et al. [16].

2. Results and Discussion D-Dimer

The statistical analysis for D-Dimer in Table 1 revealed a substantial increase (P< 0.05) when comparing acute leukemia patients to controls, as the mean of D-Dimer for patients with acute leukemia and controls (1586.492 and 219.451) ng /ml, respectively. As the mean for D-Dimer (1942.305 and 1521.798) ng /ml, respectively, significant increased (P < 0.05) in patients with acute leukemia who had a bacterial infection versus patients with acute leukemia who did not have a bacterial infection.

Table 1: D-Dimer (ng/ml)

Patients of Leukemia		Control	P value
Infection	Mean ± SD(ng/ml)	Mean ± SD	
Without bacterial infection	1521.798 ± 210.717	219.451 ± 15.992	0.0001**
With bacterial infection	1942.305 ± 256.233		0.0001**
Total	1586.492 ± 217.481	219.451 ± 15.992	0.0001**
P value	0.0001**		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

The majority of patients' D-dimer levels were found to be elevated when they were first diagnosed, regardless of the type of acute leukemia. However, once complete remission was achieved, The initial high D-dimer plasma concentration was much lower. Furthermore, in the majority of cases of relapse or resistance to treatment, a rise in D-dimer plasma concentration is seen [15]. According to one study, D-dimer (DD) and other coagulation markers are significantly elevated during sepsis, particularly when disseminated intravascular coagulation occurs (DIC). As a result, D-Dimer has been investigated as a possible risk marker in infected patients [16]. A customized drug aimed at reducing coagulation activation and/or enhancing fibrinolysis might assist septic patients with poor DD and a high mortality risk, according to a prior study. DIC is a potentially fatal sepsis complication. The fibrin-related marker D-dimer is the most commonly used to diagnose DIC. Coagulation and fibrinolysis, on the other hand, have an impact on DD

levels. Individuals with severe sepsis and normal DD had a greater death rate. In sepsis, normal DD is thought to hide a DIC type with substantial fibrinolysis inhibition [17]. And some literatures disagreement with our results about the correlation between D-Dimer and sepsis. Although some studies have linked higher D-Dimer values to worse clinical outcomes, others have not, implying that DD's predictive usefulness in sepsis patients may be limited or poor [18]. A recent study indicated that sepsis patients with D-Dimer concentrations that were slightly or significantly higher than the normal reference range had a nearly 4-fold higher chance of dying than those with DD concentrations that were slightly or significantly lower [17].

Platelets (PLT)

Table 2 shows a substantial (P< 0.005) drop in the mean of PLT in patients with acute leukemia as compared to controls, with the mean of PLT for Leukemia patients and controls (132.826 and 257.04) µl, respectively. As the mean of PLT (110.125 and 136.954) µl, respectively, Patients with acute leukemia with bacterial infection had a non-significant decrease (P > 0.05) when compared to those with acute leukemia without bacterial infection.

Table 2: PLT (µl)

Patients of Leukemia		Control	P value
Infection	Mean ± SD(µl)	Mean ± SD	
Without bacterial infection	136.954 ± 103.106	257.04 ± 62.334	0.0001**
With bacterial infection	110.125 ± 95.166		0.0001**
Total	132.826 ± 101.946	257.04 ± 62.334	0.0001**
P value	0.3353		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

In the hematological system, acute leukemia is a common malignant tumor. It frequently results in unusual bleeding and, as a result, death. Leukemia-related bleeding is a complicated mechanism that includes leukemic cells infiltrating the artery wall, platelet production loss, and coagulation/anticoagulation failure. The most common reasons of bleeding in AL are a quantitative decrease and qualitative malfunction of platelets [19]. Platelets release a range of substances that can stimulate or inhibit leukemic cell proliferation, according to research; consequently, Their activities are anticipated to be extremely context-dependent on the kind and expression of leukemia receptors, the stage of disease, and the leukemic environment [20]. According to a few studies, platelets, they are implicated in sepsis etiology and contribute to sepsis outcomes as important effector cells in both haemostasis and inflammation. Hyperinflammation, disseminated intravascular coagulation, and microthrombosis are all caused by platelets, and they all lead to multiple organ failure. Platelet activity and buildup are important factors in sepsis-related consequences like acute lung and renal impairment. Platelet activation readouts could be used to detect sepsis early on, and platelet inhibition appears to be a key target for immune-modulating therapy in septic patients [21]. As a result of their involvement in both inflammation and thrombosis, platelets contribute to an excessive inflammatory host response during sepsis and enhance the onset and progression of sepsis. Platelets, on the other hand, have a receptor- and organ-dependent ability to reduce inflammation and promote tissue repair. As a result, the outcome is governed by the balance of platelet pro-inflammatory and anti-inflammatory functions [22].

Prothrombin Time (PT)

The period of PT in acute leukemia patients was not significantly shorter (P > 0.05) than in controls, according to the results of statistical analysis in Table 3, as the period of PT for acute leukemia patients and controls (14.801 and 15.264, respectively) In the same Table, the results showed that the mean of PT (13.95 and 14.956, respectively) decreased insignificantly (P > 0.05) When patients with acute leukemia with bacterial infection were compared to those with acute leukemia without bacterial infection, they had a higher survival rate.

Table 3: PT (sec.)

Patients of Leukemia		Control	P value
Infection	Mean ± SD(sec.)	Mean ± SD	
Without bacterial infection	14.956 ± 2.021	15.264 ± 2.938	0.4685
With bacterial infection	13.95 ± 1.880		0.0983
Total	14.801 ± 2.024	15.264 ± 2.938	0.2556
P value	0.0672		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

Coagulation assays revealed a prolonged prothrombin time (PT), a normal activated partial thromboplastin time (aPTT), and a slightly elevated fibrinogen level in AML patients [23]. There were also disagreements with a study that showed Intracranial hemorrhage (ICH) is caused by hypertension, vessel wall abnormalities, low platelet count, platelet dysfunction, coagulation factor deficiency, disseminated intravascular coagulation (DIC), sepsis, and hyperleukocytosis in patients with hematological malignancies [24]. Other investigations have found that When evaluating sepsis-related coagulopathy, According to the International Society of Thrombosis and Haemostasis, researchers should combine the PT ratio with a platelet count, fibrin-related indicators such soluble fibrin, fibrin degradation product (FDP) or D-dimer, and fibrinogen, as is commonly done in cases involving an overt DIC score [25].

3. Conclusion

Our results of this research indicated to present relationship between D-Dimer and sepsis in acute leukemia patients, while PLT and PT not related with sepsis but these parameters indicated to diagnosis and progression of leukemia disease.

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