Immunological and Serological Parameters of Leukemia's Patients and Associated with Bacterial Infections

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Abstract

Objective: Our research aims to evaluate correlation between WBC,IL-6, CRP 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 immunological and serological parameters must be determined (WBC,CRP and IL-6).

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 WBC(12.350) 103/ µl, CRP (45.031) mg/l, and IL-6(36.498) pg/Ml. In acute leukemia without bacterial infection there were some correlation between some parameters CRP and IL-6 in addition to a positive correlation (0.612). There were some differences in correlation measures in acute leukemia with bacterial infection, such as IL6 and WBC, as it was positive correlation (0.639).

Conclusions: the study were investigated high level of WBC, CRP and IL-6 in leukemia patients with bacterial infections.

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 myeloblastic leukemia (AML)

Acute lymphoblastic leukemia (ALL) [2].

Acute myeloid leukemia (AML) is a bone marrow-related kind of leukemia. Clonal proliferation and differentiation arrest of myeloid progenitor cells characterize 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]. In the United States (US), the annual incidence of AML 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 the appearance of more than 30% lymphoblasts 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]. 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 [7]. 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 [8]. 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-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 [9, 10]. Gram-negative bacteria were the most common pathogens in acute leukemia patients [9]. Synthesized in the liver and secreted in response to interleukin 6, C-reactive protein (CRP) is commonly used to diagnose and follow patients in several infectious scenarios or other systemic inflammatory disorders. CRP was shown to precede the occurrence of fever in patients with BSI. There is some evidence that it may

doi.org/10.31838/hiv22.02.250 Received: 19.04.22, Revised: 20.05.22, Accepted: 15.08.22

serve as a surrogate marker preceding fever, sepsis and blood-stream infections in immunocompromised patients [11].

2. 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 [12].

The patient's identification had been established and 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, syringe, as needed for a blood culture (10 mL), Sharps waste disposal container, sterile gloves, tourniquet, adhesive strip, povidone iodine or alcohol solution (or other acceptable 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. The hands were then cleansed or rubbed until they were completely 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.The blood culture site was covered with a green sterile cover with an opening.

A needle was used to puncture the blood vessel of the patient, 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. After cleaning the lid of the blood culture container with an alcohol swab, inoculate blood into the culture bottle if the blood was not drawn directly into the culture bottle using the vacutainer method before collecting blood for further 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 BacT/ ALERT® 3D system (bioMeriéux, Marcy l'Etoile, France) was utilized to evaluate the blood cultures. Before being incubated at 35°C in a 5% CO2 environment, the bacteria were collected and placed on blood agar plates (BAP; Asan Pharmaceutical Co., Ltd., Seoul, Korea) and MacConkey agar plates (Becton Dickinson, Sparks, MD, USA).And automated analysis to immunological and serological test were BIOBASE auto chemistry analyzer device to assess CRP using the method of Young [13], swelab to evaluate CBC was followed by Joshi et al. [14],and MAGLUMI to assess IL-6.

Results and Discussion

White blood cells (WBC)

Table 1's data was statistically analyzed, revealing a significant difference in the mean WBC in acute leukemia patients compared to controls ($P \leq 0.05$), with the mean WBC for acute leukemia patients and controls (12.350 and 6.792), 103/ µl, respectively. The mean of WBC increased insignificantly ($P < 0.05$) for Leukemia's patients in the case of infection with bacteria than if they were not infected with bacteria, as the mean of WBC was (14.823 and 11.903) 103/ µl, respectively.

Table 1: WBC count (103/ µl)

Patients of Leukemia		Control	P value
Infection	Mean ± SD(103/ µl)	Mean ± SD	
Without bacterial infection	11.903 ± 2.133	6.792 ± 1.346	0.0001**
With bacterial infection	14.823 ± 2.799		0.0001**
Total	12.350 ± 2.235	6.792 ± 1.346	0.0001**
P value	0.0001**		

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

Acute leukemia is a bone marrow disease that occurs rbwhen an abnormal white blood cell duplicates itself forever. These cells aren't doing their job, which is to combat infections. They block the generation of other normal blood cells in the marrow as they amass, leading in anemia, bleeding, and recurring infections. The leukemic cells divide and may develop tumors as they migrate through the bloodstream, causing damage to organs such as the kidney and liver [14]. Leukopenia is not often acknowledged as a normal reaction to infection, despite the fact that both leukocytosis and leukopenia are considered Systemic Inflammatory Response Syndrome criteria. They wanted to see if leukopenia had any predictive value as a sepsis marker. -identification of hematological organ failure. In patients with a potential infection, they hypothesized that leukopenia would be linked to a higher death risk than leukocytosis [15]. Our results accordance with

another study that indicated that White blood cells total (WBCs) drop modestly old people, according to another study. The number of WBCs increases in response to an acute infection, and it increases dramatically in sepsis. There have been some findings that a higher number of WBCs can be a predisposing factor for bacteremia. There appears to be a relationship between neutrophilia and leucopenia and a higher risk of death in the elderly [16].

C-Reactive Proteins (CRP)

As indicated in the statistical analysis of Table 2, the mean of CRP of patients with acute leukemia was substantially higher (P < 0.005) than the control, as the mean CRP in patients with leukemia (45.031 and 11.666) mg\I, respectively. Patients with acute leukemia with bacterial infection had a higher mean CRP (58.987 vs. 42.494) than those with acute leukemia without bacterial infection, statistical analysis revealed insignificant increased (P > 0.05) in patients with acute leukemia with bacterial infection.

Table 2: CRP (mg\I)

Patients of Leukemia		Control	P value
Infection	Mean ± SD(mg\I)	Mean ± SD	
Without bacterial infection	42.494 ± 36.025	11.666 ± 6.024	0.0001 **
With bacterial infection	58.987 ± 44.743		0.0001 **
Total	45.031 ± 37.731	11.666 ± 6.024	0.0001 **
P value	0.1081		
* means significance differences (P <0.05) ** means high significances differences (P <0.001)			

Changes in plasma CRP levels can help diagnose bacterial infections [17]. CRP levels were substantially greater in acute leukemia patients with normal temperatures than in the control group. This means that even when their temperature is normal, leukemia patients are always infected, inflamed, and have a neuroendocrine system dysfunction. Some leukemia patients have a high CRP level, indicating that they were infected with bacteria or that they were inflamed by the disease itself [18]. Agreement with previous study demonstrated that According to some research, CRP shows promise in determining the severity and prognosis of sepsis. CRP levels in the blood have been linked to the severity of infection [19].In another study showed CRP is a valuable biomarker for monitoring therapy response [20].

Proinflammatory Cytokine Interleukin -6 (IL-6)

According to the statistical analysis' findings in Table 3, Significant differences were found (P < 0.05) in the concentration of IL-6 in patients with leukemia compared to the control (36.498 and 3.059), respectively. The concentration of IL-6 in acute leukemia patients infected with bacteria compared to acute leukemia patients not infected with bacteria, as well as the rate of IL-6 (76.748 and 29.180), respectively, showed significant differences (P < 0.05).

Table 3: IL-6 (pg/Ml)

Patients of Leukemia		Control	P value
Infection	Mean ± SD(pg/Ml)	Mean ± SD	
Without bacterial infection	29.180 ± 6.103	3.059 ± 0.797	0.0001**
With bacterial infection	76.748 ± 11.110		0.0001 **
Total	36.498 ± 7.240	3.059 ± 0.797	0.0001**
P value	0.0001 **		
* means significance differences (P <0.05) ** means high significances (P <0.001)			

Inflammatory cytokines such as granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-1 (IL-1), tumor necrosis factor– (TNF), IL-6, C-X-C motif chemokine 12 (CXCL2), and C-C motif chemokine ligand 3 (CCL3) can be produced by AML blasts, which reduce the colony-forming potential of normal CD34+ cells and induce endosteal endothelial remodeling and progenitor depletion [21]. Previous research has suggested Dysregulated cytokine expression, a common feature of chronic inflammation and auto-inflammatory illnesses, could have a role in the evolution of hematological malignancies, according to new research. Interleukin-1 (IL-1) and Interleukin-6 (IL-6) are pro-inflammatory cytokines that influence hematopoietic cell activity and produce inflammation [22]. Another study shows Clinically significant IL-6 levels have recently been shown to be in the range of 5-25 pg/mL in physiologically normal circumstances and up to 1000 pg/mL in sepsis patients [23].

3. Conclusion

our results of this research indicated to present relationship between WBC,IL-6,CRP and sepsis in acute leukemia patients, These parameters can be considered as most important biomarkers for patients with sepsis addition to high temperature and febrile neutropenia

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