



Original Article

Evaluation of Inflammatory Markers (PV, ESR, CRP) in the Early Diagnosis of Cancer and Their Relationship With Survival Rate



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ABSTRACT

**Introduction:** This study investigates the prevalence of cancer, compares inflammatory factors, and examines how inflammatory markers—C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and plasma viscosity (PV)—can aid in the early diagnosis of cancer in primary care settings.

**Materials & Methods:** We included newly diagnosed patients of all types of malignancy (children and adults) in this retrospective study from 2018 to 2023. The results of CRP, ESR, PV tests, and demographic data (age, gender, type of malignancy, and survival) were collected. Research data were analyzed using the t-test and chi-square statistical methods. According to the results, the average ESR and PV were higher in patients who died than in those who survived ( $P < 0.05$ ). In addition, it was shown that there was a significant relationship between the age and gender of the patients and their survival ( $P < 0.05$ ). It was also shown that there was a significant relationship between the survival of patients with ESR, CRP, and PV across different cancers ( $P < 0.05$ ). On the other hand, a significant correlation was found between ESR, CRP, and PV among different cancers ( $P < 0.05$ ).

**Results:** Based on the results, it was shown that the average ESR and PV were higher in patients who died than in those who survived ( $P < 0.05$ ). In addition, it was shown that there was a significant relationship between the age and gender of the patients and their survival ( $P < 0.05$ ). It was also shown that there was a significant relationship between the survival of patients and ESR, CRP and PV across different cancers ( $P < 0.05$ ). On the other hand, it was shown that there was a significant correlation between ESR, CRP and PV among different cancers ( $P < 0.05$ ).

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⋮ **Conclusion:** To halt the progression of acute inflammation to chronic inflammation and mitigate its harmful implications, it is essential to reduce the inflammatory response. Efficient management of inflammation is crucial in preventing patient mortality and is thus essential for the treatment and survival of patients with malignancies.

## 1. Introduction

In recent years, we have witnessed an increasing trend in cancer incidence in all parts of the world. In Iran today, after cardiovascular diseases and traffic accidents, cancer is the third leading cause of death. The increasing number of cancer patients, both globally and in our country, has elevated the issue to a public health concern [1].

Various factors may cause cancer, making it a fatal disease. Numerous studies demonstrate the role of chronic inflammation in cancer development and even the spread of malignancy to nearby tissues (metastasis). Inflammation causes the release of modified cells, which multiply autonomously and suppress the DNA repair system [2]. Early diagnosis of cancer is very important. Many early symptoms are non-specific, and sometimes it is difficult to distinguish them from the symptoms of benign diseases. The most common inflammatory marker tests are C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and plasma viscosity (PV) [3].

As part of the body's inflammatory reaction, blood vessels become more permeable, which alters blood flow. Additionally, proteins, fluids, and white blood cells (leukocytes) are redirected from the bloodstream to the injured area. Inflammation may be either acute or chronic, with the former being a temporary reaction. Inflammation has the potential to harm tissues in certain situations. It is the immune system's reaction to its own tissues that leads to chronic inflammation. Considering the specifics of cancer patients' cases, inflammatory variables are vital in establishing the extent of the illness and aiding in diagnosis [4].

More than 25 percent of cancer deaths are due to chronic inflammation. Inflammation causes the continuation and progression of cancer, changes in the state of tumor tissue, angiogenesis (the angiogenic process), and metastases, and prevents the suppression of the anti-cancer immune response. Inflammation can cause genetic damage by producing oxidative compounds, such as reactive oxygen and nitrogen species, leading to gene mutations, the formation of toxic substances, and DNA instability. The functional states of CRP isoforms indicate a com-

plex relationship between their response during early inflammation related to tumorigenesis and disease progression. Monomeric CRP's activity in the acute phase response shows how well it matches the components and signaling pathways of a tumor environment that is actively growing [5].

## 2. Material and Methods

### 2.1. Data collecting

This retrospective study included patients newly diagnosed with all types of malignancy (children and adults) from 2018 to 2023. The data collected included CRP, ESR, and PV test results, along with demographic data (age, gender, type of malignancy, and survival status). The statistical analysis was performed using t-tests and chi-square tests to determine significant differences.

### 2.2. Methodology

**CRP measurement:** CRP levels were measured qualitatively using an indirect agglutination method. The results were categorized as negative, +1, +2, +3, and +4.

**ESR measurement:** ESR was determined using the Westergren method, with measurements recorded after one hour using a standard device.

**PV:** PV was measured using a standard viscometer.

## 3. Results

In this retrospective study, conducted during 2018–2023, newly diagnosed patients with all types of malignancy (children and adults) were included in the research. The results of CRP, ESR, and PV tests, along with demographic data (age, gender, type of malignancy, and survival) were collected. Research data were analyzed using the t-test and chi-square statistical methods. The CRP measurement method was performed qualitatively using the indirect agglutination method, and the results were reported as negative, +1, +2, +3, and +4. ESR was measured using the Westergren method, and the results were obtained within an hour with the help of a device. PV data was obtained using a viscometer.

In this study, 636 patients whose malignancy was newly diagnosed were examined retrospectively in terms of inflammatory factors such as PV, ESR, and CRP over a 5-year period from 2018 to 2023. The overall average age of adult patients was  $32.15 \pm 26.79$  years, and that of children was  $5.91 \pm 6.51$  years. Of the total, 359 patients (56.4%) were adults, and 277 patients (43.6%) were children. In terms of gender, 323 patients (50.8%) were female and 313 (49.2%) were male. In terms of survival, the results showed that 190 patients (29.9%) were alive, 170 patients (26.7%) had died, and 276 patients (43.4%) had partial treatment (full treatment had been completed, and until the time of the study, they remained on life support). In terms of CRP, 436 samples (68.6%) were positive, and 200 samples (31.4%) were negative. The average ESR was  $60.31 \pm 32.58$ . The average PV was  $1.72 \pm 0.07$  (Table 1).

### 3.1. Evaluation of patient survival based on age and gender of patients:

100 adults and 176 children received partial treatment. In the group that survived, 123 patients were adults, and 67 patients were children. In the group that died, 136 patients were adults, and 34 patients were children. This relationship was investigated using chi-square analysis,

and a significant difference was observed in the survival outcomes between adults and children ( $P < 0.001$ ).

In the group of patients receiving partial treatment, 156 were women and 120 were men. In the group that survived, 84 patients were adults, and 106 patients were children. In the group that died, 83 patients were adults, and 87 patients were children. We investigated this relationship using chi-square analysis. Males and females showed a significant difference in survival outcomes ( $P = 0.028$ ) (Tables 2 and 3).

### 3.2. Evaluation of the effect of increased inflammatory factors and type of malignancy on survival in two groups of patients (children and adults) with malignancies

The most common types of malignancy in adults were breast cancer, Hodgkin's lymphoma, and gastrointestinal cancers, respectively. In children, the most common type of malignancy were leukemia and brain-spinal tumors. Based on the type of malignancy, the increase in inflammatory factors, and the effect on the survival rate, adult and child patients were evaluated. In adults, liver cancer and brain tumors were the most lethal types of malignancy, while in children, AML was the most lethal (Tables 4 and 5).

**Table 1.** Demographic and laboratory information of patients with malignancies referred to Begai 2 Hospital from 2018 to 2023 (n=636)

Variables		Median±Mean/No. (%)
Age of adult patients		32.15±26.79
Age of pediatric patients		5.91±6.51
ESR		60.31±32.58
PV		1.72±0.07
Age group	Adult	359(56.4)
	Pediatric	277(43.6)
Sex	Female	323(50.8)
	Male	313(49.2)
Survival rate	Partial treatment*	276(43.4)
	Live	190(29.9)
	Death	170(26.7)
CRP	Pos.	436(68.6)
	Neg.	200(31.4)

\*Complete treatment had been completed, and they were alive at the time of the study.

**Table 2.** Correlation between the survival of patients suffering from malignancies referred to Begai Hospital 2 with mean ESR and PV during 2018 to 2023

Marker	Survival	No.	Mean±SD	Lowest	Highest
ESR	In treatment	276	60.264±32.914	1	129
	Live	190	55.916±29.952	1	120
	Death	170	65.3±34.282	1	121
PV	In treatment	276	1.708±0.073	1.31	1.81
	Live	189	1.723±0.058	1.29	1.81
	Death	169	1.747±0.053	1.29	1.82

In this study, there was a significant correlation between CRP results and the survival rate of patients ( $P<0.05$ ). The lower the CRP level at the beginning of the treatment, the better the response to the treatment and, thus, the survival of the patients.

#### 4. Discussion

Researchers have pointed out the important role of this inflammatory protein in the prognosis of cancers, including breast cancer. Generally, CRP level can be used as a prognostic factor to predict the survival of cancer patients [7].

In the present study, using chi-square analysis, a significant difference was found between positive CRP results and types of cancer ( $P<0.001$ ). Researchers found that the level of CRP in patients with different cancers varied. This led to the discovery that cancer patients with higher levels of inflammation also had higher average CRP levels [8]. Liu et al. stated that an increase in CRP levels in patients may increase the risk of malignancy, and its decrease may be associated with a decrease in gastrointestinal cancer [9]. Juan et al.'s study revealed a higher average CRP level in leukemia patients compared to

those with solid tumors. In addition, their results showed that the average CRP level was higher in patients with autoimmune diseases compared to cancer patients [10].

The results of the present study showed that the average PV in patients who died and those who received partial treatment was higher compared to patients who survived, and this difference was statistically significant ( $P<0.05$ ).

Jang et al.'s study demonstrated that an increase in PV in patients can lead to increased metastasis and decreased patient survival [11]. Conversely, Shimolina et al.'s study elucidated that an increase in PV in patients led to an increase in chemotherapy resistance and a decrease in patient response to treatment [12].

The present study observed a significant relationship between the age and sex of patients and the survival rate, with different survival and mortality percentage of in adults compared to children. Afshar et al.'s study demonstrated that an increase in patient age is associated with a decrease in the survival rate, depending on the type of cancer. In other words, it was shown that increasing age can be one of the factors contributing to poor progn-

**Table 3.** Correlation between the survival of patients suffering from malignancies referred to Begai 2 Hospital and CRP levels during 2018 to 2023

Survival	No. (%)		
	Pos.	Neg.	Total
In treatment	181(41.51)	95(47.5)	276(100)
Live	125(28.67)	65(32.5)	190(100)
Death	130(29.82)	40(20)	170(100)
Total	323(50.79)	313(49.21)	636(100)

**Table 4.** The effect of the increase in inflammatory factors and type of malignancy on survival in adult patients admitted to Begai 2 Hospital during 2018 to 2023

Type of Cancer	No.	Survival	%		
			CRP+	ESR	PV
Brest cancer	29	46.35	61.53	53.84	37.76
Uterine cancer	3	100	0	0	Normal
Ewing sarcoma	4	100	100	100	Normal
Colon/rectal cancer	17	59	70	90	90
AML	13	20	98	100	40
ALL	10	20	80	85	20
CLL	5	50	50	50	18
Ovarian cancer	4	100	70	70	Normal
Lymphoma	22	55	40	40	40
Bladder	3	100	50	90	50
Esophagcal cancer	5	100	48	48	27
Osteosarcoma	1	100	100	100	100
Gastrointestinal cancer	12	90	79	100	49
HCL	11	90	78	90	49
Multiple Myeloma	6	100	67	100	80
Pancreas cancer	7	80	50	90	20
Testis	1	100	50	100	50
Liver	100	50	0	4	4
Esophagus	7	30	70	80	70
Lung	7	50	67	67	50
Skin	1	100	0	100	100
Prostate	2	90	0	58	28
Brain	1	0	100	0	100

sis in patients and may lead to a decrease in survival. In addition, their results showed that, in terms of gender, women had a greater decrease in survival compared to men [13]. Dong et al.'s study demonstrated that the survival rate of patients varies by age and gender for various cancers. This revealed that women are more likely to suffer from certain cancers, like breast cancer, while men are more likely to suffer from brain tumors. In this research, the survival rate of men suffering from malignancies was lower compared to women [14]. Radkiewicz et al.'s study revealed that men had a lower survival rate

than women, and older patients had a lower survival rate than younger patients [15].

The results of this study showed that men with malignancies have a lower survival rate than women. Furthermore, the patient age was associated with resistance to treatment and fewer recovery symptoms. Additionally, a significant correlation was observed between the patient survival and different cancer types. In terms of mean ESR and mean PV, significant correlations were also observed across different cancers.

**Table 5.** The effect of increased inflammatory factors and type of malignancy on survival in pediatric patients admitted to Begai 2 Hospital from 2018 to 2023

Type of Cancer	No.	Survival	%		
			CRP+	ESR	PV
Lymphoma	58	97	77	94	60
Wilms tumor	30	97	79	88	50
Ewing sarcoma	16	100	86	94	18
Neuroblastoma	25	90	75	100	68
AML	21	5	98	100	79
ALL	69	80	85	94	43
Rhabdomyosarcoma	18	100	83	83	28
Spinal Cord Tumor	23	100	49	57	11
Kidney	18	100	50	50	45

Numerous studies has shown that the averages of inflammatory markers—including mean ESR—in patients with various cancers vary. Therefore, the average ESR in different types of cancer can be different from each other. According to studies, the average viscosity of plasma in patients varies based on blood cell count and type of cancer [15].

In the present study, the results showed that there was a significant difference between the amounts of PV in different types of cancer using the analysis of variance method ( $P=0.002$ ). PV is an important index in cancer patients that can be used as a primary diagnostic factor and to help predict the course of the disease [16].

Therefore, an increase in PV can be associated with a decrease in patient survival. Furthermore, studies have demonstrated that patients with various cancers exhibit varying PV. PV increases in leukemia patients. Along with the number of blood cells [17].

In the present study, using the analysis of variance method, a significant difference was observed between the ESR levels in different types of cancer ( $P<0.001$ ). Kornum et al.'s study demonstrated a correlation between the average increase in ESR in leukemia patients and an increase in patients with kidney, liver, and adrenal gland cancers [18]. The results of this research show that, using chi-square analysis, significant differences were observed between survival rates and cancer types ( $P<0.001$ ).

Researchers believe that the survival of patients with different cancers varies. This difference can be caused by the type of cancer, the progression of the disease, and the clinical condition of the patient. Based on this, it has been shown that the detection of cancer in the early stages of diagnosis, along with timely treatment, improve the survival of patients, and if the cancer is detected in the advanced stages, it is associated with a decrease in the survival of patients and an increase in their mortality rate [19]. Inflammatory illnesses may be better prevented and treated with a deeper knowledge of the pathways and processes that make up the inflammatory response.

Among the limitations of this research are that, due to the retrospective nature of this study, the laboratory results of some patients were incomplete, so they were excluded from this review, and only the complete data of newly diagnosed patients were included in the study.

When the body's first reaction to tissue damage, which is referred to as acute inflammation, is unable to bring about a resolution of the condition, chronic inflammation follows. Cardiovascular disease, atherosclerosis, type 2 diabetes, rheumatoid arthritis, and different types of malignancies are among the many diseases that may be accelerated by this chronic inflammation. Inflammation has been widely acknowledged as a primary catalyst for illness. Roughly 15% of all human cancers have a connection to infection and persistent inflammation. The heart, pancreas, liver, kidney, lungs, brain, digestive system, and reproductive system tissues are all vulnerable to inflammation, whether it's chronic or acute [20-25].



## 5. Conclusion

This study examined a variety of cancers and found a correlation between patients' gender and survival. Conversely, the study revealed a negative correlation between the age of patients and their survival rate. In other words, the older the patient, the lower the survival rate. To prevent acute inflammation from progressing into chronic inflammation and inflicting more harm on the tissues, it is essential to inhibit the inflammatory response. If well managed, the treatment of inflammation can prevent patient death, suggesting that the control of inflammation plays a crucial role in patient treatment.

## Ethical Considerations

### Compliance with ethical guidelines

This study was approved by the research Ethics Committee of **Jundishapur University of Ahvaz**, Ahvaz, Iran (Code: IR.AJUMS.REC.1402.471).

### Data availability

The authors confirm that the data supporting the findings of this study are available within the article.

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### Authors' contributions

Conceptualization and study design: Roya Salehi Kahyesh and Ahmad Halakou; Data collection and writing the original draft: Arta Farhadi Kia, Emir Yiğit Perk, and Mahshid Ahani; Data analysis: Saeid Bitaraf; Review and editing: Arta Farhadi Kia and Roya Salehi Kahyesh; Final approval: All authors.

### Conflict of interest

The authors declared no conflict of interest.

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