Evaluation of inflammatory markers (PV_ESR_CRP) in early diagnosis of cancer and its relationship with survival rate

Abstract

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

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, Plasma Viscosity tests, and demographic data (age, gender, type of malignancy, and survival) were completed. Research data were analyzed using t-test and Chi-Square statistical methods. According to the results, the average ESR and plasma viscosity were higher in patients who died than in patients 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 plasma viscosity in different cancers (p<0.05). On the other hand, it was shown that there was a significant correlation between ESR, CRP, and plasma viscosity between different cancers (p<0.05).

Based on the results, it was shown that the average ESR and plasma viscosity were higher in patients who died than in patients who survived (p<0.05). In addition, it was shown that there was a significant relationship between the age and gender of the patients with their survival (p<0.05). It was also shown that there was a significant relationship between survival of patients with ESR, CRP and plasma viscosity in different cancers (p<0.05). On the other hand, it was shown that there was a significant correlation between ESR, CRP and plasma viscosity between different cancers (p<0.05).

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.

key words: inflammatory markers, PV, ESR, CRP, early diagnosis, cancer

1. Introduction

In recent years, we have witnessed an increasing trend of cancer in all parts of the world. In Iran today, after cardiovascular diseases and accidents, cancer is the third 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).

1.1Objective.

Various factors may cause cancer, making it a fatal disease. Numerous studies demonstrate the role of continued 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 acute phase protein C (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 more transient 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 persistent 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 (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, causing gene mutations, producing, and forming toxic substances, or causing DNA instability. The functional states of CRP isoforms

indicate a complex relationship between its 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 needed parts 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 plasma viscosity test results, along with demographic data (age, gender, type of malignancy, and survival rates). 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.

Plasma Viscosity: Plasma viscosity was measured using a viscometer.

3. Results

In this retrospective study, during 2018–2023, newly diagnosed patients of all types of malignancy (children and adults) were included in the research. The results of CRP, ESR, Plasma Viscosity tests, and demographic data (age, gender, type of malignancy, and survival) were completed. Research data were analyzed using t-test and Chi-Square statistical methods. The CRP measurement method was done qualitatively and by 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 the device. Plasma viscosity data was obtained using a viscometer. Results In this study, 636 patients whose malignancy was newly diagnosed were examined retrospectively in terms of

inflammatory factors such as plasma viscosity, ESR, and CRP over a 5-year period from 2018 to 2023. The overall average age of adult patients was 32.15 ± 26.79 years, and in children it was 5.91 ± 6.51 years. 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%) died, and 276 patients (43.4%) had partial treatment (full treatment was performed, and until the time of the study, they were under 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 ± 32.58. The average plasma viscosity was 1.72 ± 0.07. (Table 1).

Table 1. Demographic and laboratory information in patients with malignancies referred to Begai 2 Hospital in the from 2018 to 2023

Variable		No: 636
Age of adult patients (median ± mean)		32.15± 26.79
Age of pediatric patients (median ± mean)		5.91± 6.51
ESR(mean ± mean)		60.31± 32.58
plasma viscosity(mean ± mean)		1.72 ± 0.07
Age group	Adult (N/ %)	359 (56.4)
	Pediatric(N/ %)	277 (43.6)
Sex (N/ %)	Female (N / %)	323 (50.8)
	Male (N / %)	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)

* Partial treatment: complete treatment was done, and they were alive until the time of study.

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 cases were adults, and 67 cases were children. In the group that died, 136 cases were adults, and 34 cases were children. This relationship was investigated using

chi-square analysis. A significant difference was seen in the type of survival of adults and children (p-value < 0.001).

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

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

ESR	Survival	No	Mean	standard deviation	Lowest	Highest
	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
plasma viscosity	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

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

Survival	Pos. (N/ %)	Neg. (N/ %)	Total (N/ %)
In treatment	181(41.51)	95(47.50)	276(100)
Live	125(28.67)	65(32.50)	190(100)
Death	130(29.82)	40(20)	170(100)
Total	323(50.79)	313(49.21)	636(100)

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

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 was leukemia and brain-spinal tumors. Based on the

type of malignancy, the increase of 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, it was AML leukemia. (Tables 4 and 5).

Table 4- The effect of the increase of 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

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

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. Tas et al. concluded in their research that an increase in CRP levels in patients led to a decrease in survival, thereby increasing the death rate (6).

4. Discussion

Researchers have pointed out the important role of this inflammatory protein in the prognosis of cancers, including breast cancer. Generally, we can use the CRP index as a prognostic factor to predict the survival of cancer patients (7).

In the present study, using chi-square analysis, a significant difference was seen between positive CRP and types of cancer (P-value < 0.001). The researchers found that the level of CRP in patients with different cancers can be different from each other. 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 can increase the risk of malignancy, and its decrease can be associated with a decrease in gastrointestinal cancer (9). Juan et al.'s study revealed a higher average CRP in leukemia patients compared to those with solid tumors. In addition, their results showed that the average CRP was higher in patients with autoimmune diseases compared to cancer patients (10).

The results of the present study showed that the average viscosity of plasma 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 plasma viscosity in patients can lead to increased metastasis and decreased patient survival (11). Conversely, Shimolina et al.'s study elucidated that an increase in plasma viscosity 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 a different percentage of survival and mortality in adults compared to children. Afshar et al.'s study demonstrated that an increase in patient age leads to 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 prognosis in patients and cause 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 according to 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's age indicates resistance to treatment and fewer recovery symptoms. Additionally, a significant correlation was seen between the survival of patients in relation to different cancers, also in terms of mean ESR, mean plasma viscosity, a significant correlation was observed between different cancers.

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

In the present study, the results showed that there is a significant difference between the amounts of PV in different types of cancer using the analysis of variance method (P-value = 0.002). Plasma viscosity is an important index in cancer

patients that can be used as a primary diagnostic factor and to predict the course of the disease (16).

Therefore, an increase in plasma viscosity can be associated with a decrease in patient survival. Furthermore, studies have demonstrated that patients with various cancers exhibit varying plasma viscosity. Plasma viscosity increases in leukemia patients as well as the number of blood cells (17).

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

Researchers believe that the survival of patients with different cancers is different. This difference can be caused by the type of cancer, the progress 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 increases the survival of patients, and if the cancer is detected in the advanced stages, it will be 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 is that, due to the retrospective nature of this study, the laboratory results of some patients were incomplete, which 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 to 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 the primary catalyst for illness. Roughly fifteen percent of all human cancers have a connection to infection and persistent inflammation. 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).

This study examined a variety of cancers and found a correlation between patients' gender factors 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 to the tissues, it is essential to inhibit the inflammatory response. If well managed, the treatment of inflammation can prevent patient death, suggesting that control of inflammation plays a crucial role in patient treatment.

Authors contribution

RSK and AH, were the major contributors to conceptualizing and formulating the research question and designing the study.

AFK, EY.P, MA, collected the data and wrote the first draft of the manuscript.

SB, analyzed the data

A F K and R S K, revised and developed the first draft based on a critical appraisal of their colleagues. All authors commented on the modified draft, and the final version of the manuscript was prepared. Finally, all authors approved the final manuscript.

Acknowledgment

Conflict of interest

The authors declare that they have no conflicts of interest related to this study.

Ethical considerations

This study was approved by the ethics code IR.AJUMS.REC.1402.471, at Jundishapur University of Ahvaz.

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