

Short Duration of Cancer and Short Duration of Cancer Treatment is associated with Elevated Serum C Reactive Protein among Cancer Patients Attending Oncology Unit at the Bugando Medical Centre Mwanza, Tanzania

Godfrida Marandu¹, Shabani Iddi^{2*}, Lucas F. Kieji³, Betrand Msemwa⁴, Mary R. Shineneko⁵, Stephen E. Mshana⁵ and Mariam M. Mirambo⁵

¹Archbishop Anthony Mayala School of Nursing, Catholic University of Health and Allied Sciences, Mwanza, Tanzania

²Department of Physiology, Weill Bugando School of Medicine, Catholic University of Health and Allied Sciences, Mwanza, Tanzania

³Department of Internal Medicine, Weill Bugando School of Medicine, Catholic University of Health and Allied Sciences, Mwanza, Tanzania

⁴Institute of Allied Health Sciences, Catholic University of Health and Allied sciences, Mwanza, Tanzania

⁵Department of Microbiology and Immunology, Weill Bugando School of Medicine, Catholic University of Health and Allied Health Sciences, Mwanza, Tanzania

*Corresponding author: Shabani Iddi, Department of Physiology, Weill Bugando School of Medicine, Catholic University of Health and Allied Sciences, Mwanza, Tanzania, Tel: +255755059621; E-mail: shabsizya2007@yahoo.co.uk

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Abstract

Background: C-Reactive protein (CRP) is an acute phase protein of hepatic origin that increases following interleukin-6 secretion by macrophages and T cells. Elevated serum levels of CRP have been associated with an increased risk of cancer and high levels have been recorded in some types of cancer. This study aimed to determine the proportion of cancer patients with elevated serum CRP and associated factors among patients with different types of cancers attending oncology unit at Bugando Medical Center (BMC) in Mwanza Tanzania.

Methods: A cross sectional hospital based study involving 200 cancer patients was conducted from May to July 2019 at BMC, Mwanza Tanzania. Sociodemographic and other relevant information was collected using structured pretested data collection tool. Semi quantitative detection of CRP was done using Agglutination test as per manufacturer's instructions. Data were analyzed using STATA version 13.0 software.

Results: The mean age of enrolled participants was 50.93 ± 19.22 years. Sixty five participants, (32.5%, 95% CI: 26.0-38.9) were found to have elevated levels of serum CRP. Short duration of cancer ($\chi^2=8.7268$, $p=0.013$) and short duration of treatment ($\chi^2=7.507$, $p=0.023$) were significantly associated with elevated serum CRP among cancer patients.

Conclusion: Elevated levels of CRP in cancer individuals is associated with short cancer duration (<3 months) and short duration of cancer treatment (<3 months) compared to those with greater than twelve months. These findings support previous studies which showed that CRP can be used as prognostic makers in cancer patients.

Keywords: C reactive protein; Cancer; Oncology; Bugando

Introduction

Plasma C Reactive Protein (CRP) is an acute-phase reactant produced by hepatocytes, and its production is regulated by Inter-Leukin-6 (IL-6) and other inflammatory cyto-kines [1]. Plasma CRP is a useful non-specific biomarker, and plasma CRP measurement is used as a screening test for organic diseases, assessment of disease activity in inflammatory conditions such as cardiovascular diseases, diabetes, inflammatory bowel diseases, autoimmune disorders, arthritis, and many cancers. The increase in CRP concentration during inflammation has long been employed for clinical purpose as marker of inflammation. CRP synthesis increases rapidly within hours after tissue injury or infection suggesting that it contributes to host defense and that it is part of the innate immune response [1].

Elevated CRP levels were used as indicators of wide varieties of conditions from the infections to cancer [2,3].

In the most prevalence studies CRP concentration were found to be elevated in patients with cancer than healthy controls or benign conditions [4]. These elevated CRP was associated with an increased risk of incident cancer of any type, lung cancer and possibly colorectal, breast and ovarian cancers [5]. This makes cancerous patients to be in higher risk of elevated serum CRP levels. CRP has also been found to be one of the prognostic factors for the proper development of cancer patients and one of the determinants of their well-being [6]. A study done in Austria reported the mean elevation of CRP levels of 0.59 mg/dl in the cancer patients with highest levels in patients of lung and pancreatic cancers and lowest in those with the carcinoma of the breast [7]. The study done in South Korea suggests that elevated levels of CRP in apparently cancer free individual may

be associated with increased mortality from all causes and cancer, in particular lung cancer in men but not in women [8]. Despite being a common marker, there is scarcity of information regarding its variations among cancer patients with different duration of treatments. This study was carried out to provide information on the levels of CRP among cancer patients with different duration of treatment at Bugando medical Centre.

Methods

Study design, study area and study period

This was a cross sectional hospital based study which was conducted from May to July 2019 at Bugando Medical Centre, oncology department. BMC serves population of about 17 million people from 8 different regions of Lake Zone. The oncology department receives patients in three days per week and each day at least 50 patients are admitted for chemotherapy and for radiotherapy; at least 20 patients are admitted in each day per week.

Sample size estimation, sampling, study population, sampling techniques and selection criteria

The sample size was estimated by using Kish Leslie 1965 formula using prevalence of 90.5%, [9] whereby the minimum sample size was 132, however, a total of 200 participants were enrolled in the study. All cancer patients in all four stages of cancer attending in oncology department at BMC during the study period were included in the study. Convenient sampling techniques were used to recruit study participants who met the inclusion criteria.

Data collection procedure

Sociodemographic and other relevant information such as age, sex, occupation, location, cancer type, duration of cancer, treatment type and duration of treatment was extracted from patient file and patient interview was collected using structured pretested questionnaire. Using a sterile procedure, 4 to 5 ml of blood specimen was collected from brachial vein in a plain vacutainer tube labelled with patient number and then transported to CUHAS multipurpose laboratory for processing.

Laboratory procedure

Blood sample was centrifuged at 3000 revolution per minute for 20 minutes to obtain serum which was then used to measure CRP. Semi quantitative detection of CRP was done using Latex agglutination method using semi quantitative test (Beacon diagnostics PVT ltd) following the standard operating procedures.

Quality control

The standard operating procedure was strictly followed for the quality assurance. Control sera both known positive and negative were performed first to check if reagents and machine were working properly before processing the samples for CRP quantification.

Data management and analysis

Data were analyzed using STATA version 13.0 software according to the objectives of the study. Categorical data were presented as proportions while continuous data were summarised as mean with Standard Deviation (SD) and median with Interquartile Range (IQR). Chi² or Fisher's exact was used to show the association of elevated CRP levels with studied factors such as age, location, cancer type, treatment type and duration of treatment. A P value of <0.05 at 95% confidence interval was considered to be statistically significant.

Ethical considerations

Ethical clearance was granted by the joint CUHAS/BMC research ethics and review committee with ethical clearance certificate number CREC/1035/2019. Permission to conduct this study was requested from hospital administration. All study participants gave a written informed consent before enrollment in the study. All patient-related information was stored carefully and anonymously using codes.

Results

A total of 200 participants with the mean age of 50.93 ± 19.22 years were enrolled in this study. More than two thirds 137 (68.50%) of the participants were female while more than a half 116 (58.00%) were from rural areas. Majority of the participants 171 (85.50%) had primary level of education while more than a half 109 (54.50%) were peasants. Other characteristics are shown in **Table 1**.

Table 1: Sociodemographic characteristics of the study participants (n=200).

Characteristics	Number	Median (IQR)/Mean(± SD)/%
Age	200	50.93(± 19.22)
Location		
Rural	116	58
Urban	84	42
Household members	200	6(IQR: 4-10)
Toilet type		
Modern	120	60
Pit latrine	80	40
Sex		
Female	137	68.5
Male	63	31.5
Education level		
Primary	171	85.5
Secondary	16	8
University/collage	13	6
Water source		
Lake/pond	84	42

Tap water	116	58
Occupation		
Employed	26	13
P/trader	30	15
Peasant	109	54
House type		
Brick/iron	153	76.5
Mud/grass	47	23.5

Prevalence of elevated serum C-reactive protein Levels and associated factors among enrolled participants

Out of 200 participants with cancer, 65 (32.5%, 95% CI: 26.0-38.9) were found with high level of CRP. On Kruskal-wallis rank sum, among of the factors tested, short duration of cancer ($P=0.013$) and short duration of treatment ($P=0.023$) were significantly associated with high level of CRP (Table 2).

Table 2: Factors associated with elevated C-reactive protein among cancer patients at BMC (n=200).

Characteristics	CRP levels (%)	Chi ²	p-value
Location			
Rural(116)	39 (33.62)	0.1381	0.691
Urban (84)	26 (30.95)		
Sex			
Female (137)	48 (35.04)	1.2755	0.259
Male (63)	17 (26.98)		
M/status			
Married (101)	31 (30.39)	0.3037	0.582
Single (99)	34 (34.34)		
Smoking			
No (194)	64 (32.99)	0.666	0.365
Yes (6)	1 (16.67)		
Arthritis			
No (199)	65 (32.66)	1.000	0.675
Yes (1)	(0.000)		
Alcohol			
No (174)	54 (31.03)	0.267	0.178
Yes (26)	11 (42.34)		
Cancer type			
No sold cancer(15)	3(20.00)	0.394	0.219

Sold cancer (185)	62 (33.51)		
Duration of cancer			
<3 months (26)	15 (57.69)	8.7268	0.013
<12 months (97)	27 (27.84)		
>12 months (77)	23 (29.87)		
Treatment type			
Other treatment (23)	11.91 (2-66.04)	5.189	0.0747
Chemotherapy (121)	3.91 (1.0-11.57)		
Radiotherapy (56)	3.3 (0.97-18.44)		
Treatment cycles			
Who has not started treatment (16)	15.35 (4.97-96.0)	8.894	0.0638
In treatment with one cycle (30)	3.23 (0.42-15.26)		
In treatment with two cycle (17)	5.05 (1.81-12.21)		
In treatment with three cycle (26)	2.05 (0.57-8.87)		
In treatment with >3 cycle (111)	4.12 (1.09-12.03)		
Duration of treatment			
In treatment <3 months (26)	13.53 (1.82-66.04)	7.506	0.0234
In treatment <12 months (97)	3.22(0.57-10.62)		
In treatment >12 months (77)	4.23(1.12-15.26)		

Levels of CRP were decreasing with the increase in duration of cancer as well as number of days on treatment (Figures 1 and 2).

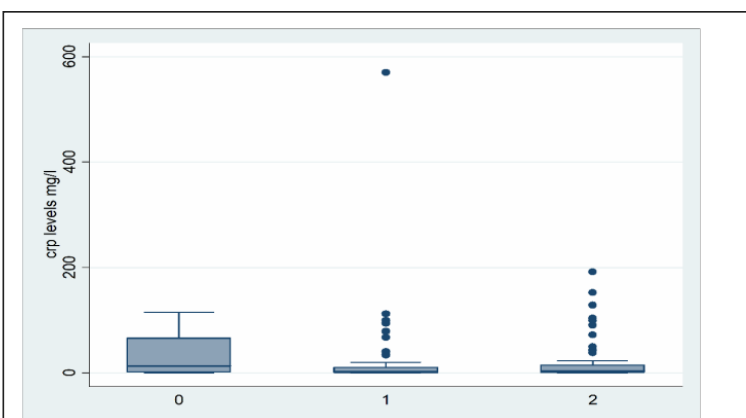


Figure 1: Relationship between CRP levels and duration of cancer (months): Levels of CRP were decreasing with the increase in the number of days of cancer.

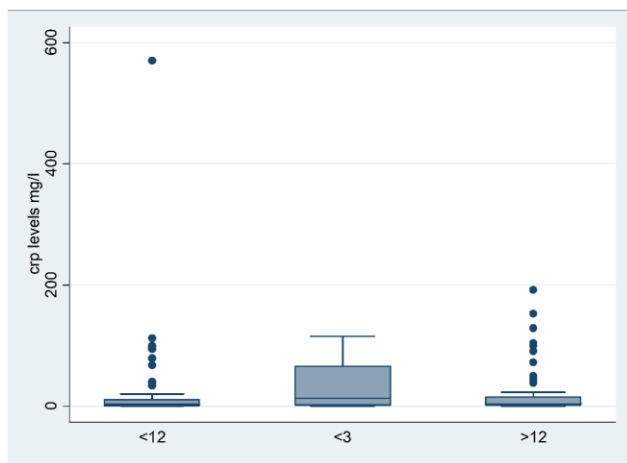


Figure 2: Relationship between CRP levels and treatment duration(months) Levels of CRP were decreasing with the increase in the number of days of treatment; those with less than three months of treatment had high level of CRP among those with more than twelve months.

Discussion

Serum C-Reactive protein (CRP) is one of the diagnostic and prognostic marker used in diagnosis and management of different diseases. Here we report the association of serum CRP levels and cancers. Prevalence of elevated CRP in cancer patients has been found in different population in different countries. In this study, the elevated CRP level was observed in 32.5% of cancer patients. This prevalence is lower compared to the studies done in other settings which observed the elevation of more than 95% in cancer patients [10]. The differences in prevalence between the current study and previous studies may be due to different population based on cancer types as well as the CRP quantification techniques.

Elevated CRP has been associated with progressive disease and decreased survival in patients with several cancers, including esophageal, gastric, colorectal, liver, pancreatic, urinary bladder, kidney, ovarian, and cervical cancers [11]. A number of epidemiologic studies have examined the association between CRP and cancer risk, and some prospective studies have shown a higher risk of developing cancer in people with elevated CRP [11].

Among of the factors studied in this population, short duration of cancers since diagnosis and short duration of treatment were significantly associated with elevated serum CRP. This is in support of the previous studies which observed CRP level to be associated with early death in newly diagnosed cancer patients with localized disease. This could be explained by the fact that, in early stages of cancer, the immune system might be stronger with increased inflammatory markers compared to later stages or with prolonged treatment. However,

as time goes on, cancer cells can develop genetic changes that help to escape the immune system and continue to proliferate.

Conclusion

In newly diagnosed cancer patients with short duration of treatment, CRP levels are likely to be more elevated, therefore can be used as prognostic marker. These findings call for the need for more studies to ascertain relationship between these findings and different types of cancer in different populations.

Conflict of Interest

The authors would like to report no existing or potential conflicts of interest.

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