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Research Article

ROLE OF HEMATOLOGICAL PARAMETERS IN DIAGNOSIS AND PROGNOSIS OF GASTRIC CARCINOMA IN KASHMIR, INDIA

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ABSTRACT

Gastric cancer is the second leading cause of death in the world. More than two-thirds of the patients are diagnosed at an advanced stage. Metastatic gastric cancer has poor prognosis with a median 5 years-survival rate of 7 %. Hematological parameters including leukocyte count, platelet count and their ratios have been used as prognostic indicators in several tumor types. The aim of the study was to examine an association of the difference in haematological parameters between gastric cancer patients and normal controls of Kashmir valley. We enrolled 210 subjects of which 110 were newly diagnosed gastric cancer cases and 100 were healthy controls. Participants were recruited from hospitals, clinics and radiology department of Shri Maharaja Hari Singh (SMHS) hospital Srinagar, India from May 2011 to Apr 2012. After informed consent, all patients were interviewed and examined and demographic and clinical information was collected. Blood samples were drawn for examination of hematological measures and for measurement of carcino embryonic antigen (CEA). We found the hematological parameters like: Hb (10 ± 2, P = 0.004), MCV (84.25 ± 5, p = 0.01), Granulocyte % (70.04 ± 10.63, p = 0.001), Lymphocyte % (26.12 ± 10.7, p < 0.0001), RDW (48 ± 10, p = 0.004) in gastric cancer patients and these were found to be highly decreased as compared to normal healthy controls where hematological parameters was in normal range. Our study was statistically significant (p < 0.005). The study suggests that the hematological parameters like HB, MCV, Granulocyte %, Lymphocyte % and RDW are decreased in gastric cancer patients and acts as an early marker in the prognosis and diagnosis of gastric cancer.

Keywords: Gastric cancer, Hematological parameters, CEA, SMHS.

INTRODUCTION

Gastric cancer being the second most common cancer, occurring worldwide year in the world[1,2]. Early disease causes minimal, nonspecific or no symptoms. Therefore prognosis for gastric cancer patients remains poor as most patients are diagnosed in advanced stages. There are definite ethnic and geographic trends in gastric cancer incidence; being high in Japan, Chile, Costa Rica, Colombia, China, Portugal, Iceland, Finland and Scotland[3], lower in US, UK, Canada, Greece, New Zealand, Sweden and Honduras[4]. Two-third of the cases occurs in the developing countries[5]. Early disease may be asymptomatic or may cause minimal, nonspecific symptoms. Therefore, prognosis of gastric cancer patients remains poor as most of the patients are diagnosed at advanced stages. Studies have shown incidence rates in men are twofold higher than those in the women. The state of Kashmir, India has an increased gastric malignancy with the frequency of 50-60 cases per 100,000 persons and 63 % of these cases occur in southern districts of Kashmir[6]. The likely reasons for higher frequency of gastric cancer are high dietary intake of meat, salt, barbeques, grilled and starchy food, smoked food and pickled foods[7]. The role of immune system on disease progression has been investigated previously and the prognostic importance of some hematological parameters including leukocyte and platelet counts, mean platelet volume (MPV) have been shown in various malignancies[9-13]. In addition, the neutrophil-lymphocyte ratio (NLR) has been reported as a simple marker of systemic inflammatory response in cancer patients[14,15]. Similarly, preoperative thrombocyte to lymphocyte ratio (TLR) has been suggested as a significant factor that predicts survival in patients with pancreatic cancer[16]. Both NLR and thrombocytosis have been reported as prognostic factors in patients with gastric cancer[19,20]. TLR and lymphocyte counts were found as prognostic factor that predicts advanced gastric cancer[21]. The evaluation of hematological parameters is easy and cost-effective in determination of prognosis and tumor response to therapy. In this study we investigated whether lymphocyte, neutrophil and platelet counts, TLR and NLR had prognostic importance in predicting the survival in metastatic gastric cancer patients.

MATERIALS AND METHODS

Subjects and Recruitment Process

This study was conducted in the Department of Biochemistry, Government Medical College, Srinagar, India from May 2011 to April 2012. We enrolled 210 subjects of which 110 were newly diagnosed gastric cancers cases and 100 were healthy age-sex matched controls. All patients were referred either from outpatient clinics or were admitted to the Shri Maharaja Hari Singh Hospital. All participants underwent a complete blood count (CBC) and measurement of CEA. The study was approved by the ethical committee of the Department of Biochemistry, Government Medical College (GMC) Srinagar, India. Individuals who fulfill inclusion criteria for this disease and gave consent to participate in the study were recruited as controls. Patients and normal were age and sex matched.

Data of the patients was obtained from medical records.

Exclusion Criteria

Patients with chronic disease such as chronic renal failure, patients who had recently received blood transfusion and those with active infection were excluded from the study.

Blood Sample Collection

About 5-6 ml of venous blood was collected, 3 ml blood was taken in EDTA vials and remaining 3 ml was centrifuged to separate serum from the cells as soon as the clot was formed.

Measurement of Hematological Parameters

The 3 ml peripheral venous blood was taken in sterilized EDTA vials. Blood samples were processed manually for various haematological indices mainly hemoglobin (Hb), total erythrocyte counts (TEC), total leukocyte count (TLC), mean corpuscular value (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), Red cell width distribution (RDW). The CBC and haemogram were assayed in Sysmex (Italy) haemocytometer analyzer. The Erythrocyte sedimentation rate (ESR) was determined by Wintrobe's method. The Hb %, RBC % and Color Index were determined by these formulae (Godkar *et al,* 2006).

Hb % = 100* Hb value / 14.5
RBC % = 100* RBC Count / 5.0
Color Index = Hb % / RBC %

Measurement of Cancer Marker

Serum aliquots were stored at 4^{o}C. The samples were allowed to thaw prior to assay, mixed thoroughly. Hemolysed and lipemic samples were rejected. CEA analysis was carried out by **e**lectro **c**hemi**l**uminescence **I**mmuno **a**ssay method using fully automatic analyzer ECLIA 2010 (Roche Diagnostic Germany).

Statistical Analysis

Data were recorded and analyzed by SPSS 16.0. The results were expressed as mean ± standard deviation (SD). Differences in variables were analyzed by t-test. The differences were considered to be significant at $p < 0.05$.

RESULTS

210 subjects participated in the research. Among which 64 % were males and 36 % were females, in the age group between 25-60 years. Reviewed hospital records were taken from were taken from Department of Biochemistry, Government Medical College, Srinagar, India. Median + Standard deviation values of Hb, RBC, WBC, MCV, RDW, Hct, Lym %, Hb %, RBC % with respect to CEA analysis were assessed and after assessment we found the hematological parameters like Hb like: Hb (10 ± 2, P = 0.004), MCV (84.25 ± 5, p = < 0.005), Granulocyte % (70.04 ± 10.63, p = < 0.0001), Lymphocyte % (26.12 ± 10.7, p < 0.0001), RDW (48 ± 10, p = 0.004) in gastric cancer patients were highly decreased as compared to normal healthy controls where haematological parameters was in normal range (table 1). Other parameters like RBC, WBC, Hct, Lym %, Hb %, RBC % were also found to be also significantly decreased in the gastric cancer patients. $p<0.05$ is statistically significant and have association in the gastric cancer disease. Also, we interviewed all the patients and controls by providing them questionnaire and information was obtained from them.

Table 1: Haematological Parameters in Gastric Cancer Patients and Healthy Controls

Hematological Parameters	Gastric cancer patients (n = 110) Mean ± SD	Normals (n = 100) Mean ± SD	P value
Hb (g / dl)	10.83 ± 2	14.72 ± 1.2	0.004
MCV	84.25 ± 5	85 ± 8.5	0.011
Granulocyte %	70.04 ± 10.63	49.60 ± 26.49	< 0.0001
Lymphocyte %	26.12 ± 10.76	39.55 ± 20.93	< 0.0001
RDW	48 ± 10	28 ± 5	0.004
RBC(10^6 / µl)	4.2 ± 0.5	5.1 ± 1.99	0.0021
HCT (%)	37 ± 2	42 ± 2	0.004
WBC (10^3 / µl)	5.18 ± 2.27	6.60 ± 1.08	0.0002
RBC (%)	79.91 ± 11.35	80.06 ± 12.14	0.0116
PLT	217.1 ± 91.60	187.5 ± 25.44	0.002
HB %	72.40 ± 11.5	75.04 ± 8.67	0.006

Comparison of haematological parameters in gastric cancer patients and normal; The results are reported in these groups as mean ± SD, which are statistically tested by Two- point ANOVA

Table 2: CEA Parameters in Gastric Cancer Patients and Healthy Controls

CEA biomarker in gastric cancer patients (N=110) Mean ± SD	CEA in Normals (N=100) Mean ± SD	P value
10.62 ± 6.54	1.842 ± 1.3	0.0132

Comparison of CEA in gastric cancer patients and normal; The Table 2 shows comparison of CEA which is used as a biomarker for detection of cancer in gastric cancer patients and in normals and p value comes to be 0.0132 which is statistically significant

Hence the decrease in hematological parameters and CEA levels are highly associated with increase in risk of developing cancer. So, assessment of these parameters would be highly beneficial for early diagnosis and thus early treatment of this disease.

DISCUSSION

Gastric carcinoma is one of the most common malignancies in the world, yet little is known about its molecular process of development and progression.Various treatments have failed to improve the survival rate in gastric cancer. Therefore, prevention and early detection of the tumor are essential to reduce cancer deaths resulting from gastric cancer. The prevalence of gastric cancer is constantly increasing, especially among men. In the present study predominant population with gastric cancers are observed in males. Cancer are frequently associated with erythrocyte abnormalities[19]. Recently the role of immune system on cancer progression was examined and leukocytes have been proposed as a diagnostic and prognostic factor in variety of cancers[10]. Previously, it was reported that pretreatment lymphocyte count had been independent prognostic factor in lung, colorectal and gastric cancer[26-29]. Low lymphocyte counts (< 1500 / mm) indicate cell-mediated immunodeficiency which

was common feature in cancer physiology, but also that is relevant prognostic role for survival[28]. The cancer related lymphopenia occur in advanced stage cancers such as small cell lung cancer, colorectal cancer and renal cell cancer[28]. Bruckner *et al*. suggested that, pretreatment lymphocyte counts of 1500 / mm and neutrophil counts of < 6000 / mm were independent prognostic factors for survival in the metastatic gastric cancer. Cancer can cause certain forms of anemia on the one hand or hyper proliferation of immature progenitors on the other hand. The anemia is usually macrocytic hypochromic and or normocytic anemia and anemia will be of moderate severity[18]. The anemia in cancer patients has been ascribed to a physiological compensation for the diminished need of tissues for oxygen. The low plasma erythropoietin levels found in cancer is in accord with this hypothesis. In our study we found hematological parameters of gastric cancer patients And compared them with normal and observed that CBC them with normal and we observed that CBC parameters levels decrease in cases like RBC, Hb, MCH, PLT Levels. and p value was found to be less than 0.05 hence study is found to be (statistically significant).

CONCLUSION

Gastric cancer has a significant influence on erythropoiesis. In view of decreased haematological parameters like Hb, RBC, MCV, HCT, RBC % and RDW in gastric cancer, it suggests that abnormal levels of these parameters might substantially influence the size variability of circulating RBC's, predisposes patient to Normocytic anemia. There might be some limitation with this study like, missing data, non-funding, less sample size, hospital based data etc. These changes need to be further should be investigated and corrected. Their presence could steer towards gastric cancer allowing its early management and thus likelihood of the disease may be decreased and also decrease in disease recurrence especially in Kashmir valley which is cancer prone area.

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Abbreviations: Haemoglobin (HB), Mean corpuscular volume (MCV), RDW (red cell distribution width)

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