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HAEMATOLOGICAL PROFILE IN HEPATOCELLULAR CARCINOMA BEFORE AND AFTER CHEMOTHERAPY

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This study was mainly performed to find out how haematological abnormalities in hepatocellular carcinoma ameliorate with the treatment. Haematological investigations were carried out in 50 clinically diagnosed patients of hepatocellular carcinoma and compared with 25 healthy control subjects. Results showed that haemoglobin (HGB), red blood cells count (RBC), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were lower while leukocytes count (WBC), platelets count (PLT) and erythrocytes sedimentation rate (ESR) were higher than normal. Then 43 patients out of 50 were reinvestigated after 5-6 months of the chemotherapeutic treatment. The results were compared with 50 patients subjected to initial haematological investigations. It was observed that HGB, RBC, HCT, MCV, MCH and MCHC tend to decrease while WBC, PLT and ESR tend to increase. Study revealed that hepatocellular carcinoma is very much resistant to chemotherapy. Various antineoplastic agents used in combination had only a palliative effect. Male patients of 60-70 years of age with blood group 'O' were observed to be more prone to hepatocelluar carcinoma.

Keywords: *Hepatocellular carcinoma; Haematology; Chemotherapy*

Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignant neoplasms. It is associated closely with cirrhosis (6,8) and its prognosis is very poor because the diagnosis is generally late, when the disease is so advanced that any effective treatment is precluded (16). Therefore, early detection is very important in the management of this cancer.

The areas in which HCC is prevalent, several surveillance programs have been performed to detect HCC in an early stage by ultrasonography and measurement of serum alpha-fetoprotein (AFP) levels (13,15,17). Ultrasonography is the most practical approach in early recognition of HCC but the ultrasonographic findings are not specific (11). AFP level is still the best tumor marker for HCC. However, not all HCC secrete AFP, and AFP level may be normal in as many as 40% of patients with early HCC and 15-20% of patients with advanced HCC (3). AFP levels may also be increased in patients with chronic hepatitis and cirrhosis(10). Therefore, more sensitive markers and newer evaluation techniques are required in detecting HCC, practically for screening a larger population at risk. Besides tumor markers and the radiological scanning, an extensive review of the haematological parameters in HCC can play an important role in the early diagnosis of hepatocellular carcinoma.

The most important drug used for the palliative treatment of HCC is doxorubicin which is given in combination with other cytostatic agents like 5-fluorouracil, cyclophosphamide and vincristine.

The aim of the study was to facilitate diagnosis, to provide a basis for future research in cancer chemotherapy with special reference to HCC, and to highlight the manner in which haematological abnormalities ameliorate with the treatment.

By keeping these facts in mind, this prospective study was carried out. Haematological parameters were investigated in HCC before and after treatment and compared with healthy control subjects.

Materials and Methods

Drug Regimen Used

1. Doxorubicin: 60-75 mg/m^2 BSA (body surface area) intravenously every 3 weeks.
2. Fluorouracil: 1 g orally on alternate days (6 doses) then 1 g weekly.
3. Vincristine: 1.5 mg/m^2 BSA intrevenously weekly.
4. Cyclophosphamide: 2-3 mg per Kg body weight per day orally.

Apparatus and Chemicals

Haematology autoanalyser (Sysmex K-1000, Toa Electronics, Japan), Coulter mixer (Coulter Electronics Limited, England).

All the chemicals and reagents were of analytical grade.

Tests Methodology

All the haematological parameters were performed by haematology autoanalyser, except ESR(2).

Patients and Methods

A total of 50 patients of hepatocellular carcinoma of which 46 were male and only 4 female were admitted to the Institute of Nuclear Medicine and Oncology, Lahore (INMOL) and Radiotherapy and Oncology Department, King Edward Medical College, Mayo Hospital, Lahore. Diagnosis was established on : Histologic evaluations (needle or surgical biopsy) or on AFP level>1000 µg/L with the specific findings of one or more of the following investigations i.e. ultrasonography, computer axial tomography, and angiography. The test population for this propective, analytical, randomized, control study was composed of patients of either sex, irrespective of age and occupation, with clinically diagnosed hepatocellular carcinoma. The patients selected were both from out patient (OPD) and wards. The population was classified in to following groups:

Cancer Group-I comprised of patients before the treatment (50 patients of hepatocellular carcinoma first investigated).

Cancer Group-II comprised of patients reinvestigated after 5-6 months of treatment (43 patients were reinvestigated while 2 died and 5 left against medical advice).

Control Group comprised of 25 healthy control subjects, irrespective of age, sex and occupation. The persons selected for this group were particularly free from any liver disease(18).

Blood Sampling: A sample of 5 ml from each patient and healthy control subject was obtained in disposable syringe containing 0.5 ml of 1% w/v ethylenediamine tetraacetic acid (EDTA) solution, of which 3 ml was diluted with 0.85% sodium chloride and placed in a westergen pipette for one hour to determine ESR (2). The remaining 2 ml blood was transferred into sample collection tube for analysing RBC, WBC, PLT, HGB, HCT, MCV, MCH and MCHC through haematology autoanalyser. After evaluating the 9 haematological paratameters for each patient and control subjects, the results were analysed biostatistically.

Results and Discussion

The mean of the readings in each group was analysed statistically and presented at the Table and Figure.

Table. Haematological investigations in healthy control subjects and in the patients of hepatocellular carcinoma before and after treatment

Test Parameters		HGB	RBC	HCT	MCV	MCH	MCHC	WBC	PLT	ESR
Normal Range		13-17.5 g/dl	4.5-5.9 x10^6/µL	41-53 %	80-100 fL	26-34 Pg	31-37 g/dl	4-11 x10^3/µL	140-400 x10^3/µL	0-15 mm/1hr
Control Group n = 25	MEAN ± S.D	13.23 ± 0.59	4.81 ± 0.21	39.95 ± 1.99	83.05 ± 1.67	27.5 ± 0.35	33.12 ± 0.6	7.47 ± 1.34	203.2 ± 20.9	6.7 ± 2.13
Cancer Group - I n = 50	MEAN ± S.D	10.85 c ± 1.83	4.08 c ± 0.69	33.6 c ± 6.2	81.93 a ± 4.06	26.62 c ± 0.73	32.41 c ± 1.61	11.33 c ± 4.27	274.6 c ± 115	41.5 c ± 8.22
Cancer Group - II n = 43	MEAN ± S.D	11.6 b ± 2.01	4.1 b ± 0.56	34 b ± 5.1	81.5 a ± 5.2	28.2 b ± 2.5	34.02 b ± 1.9	10.1 a ± 4.1	259.1 a ± 88.8	36.73 a ± 6.94

a)Not significant (P>0.05), b)Significant (P>0.05), c)Highly significant (P>0.01)

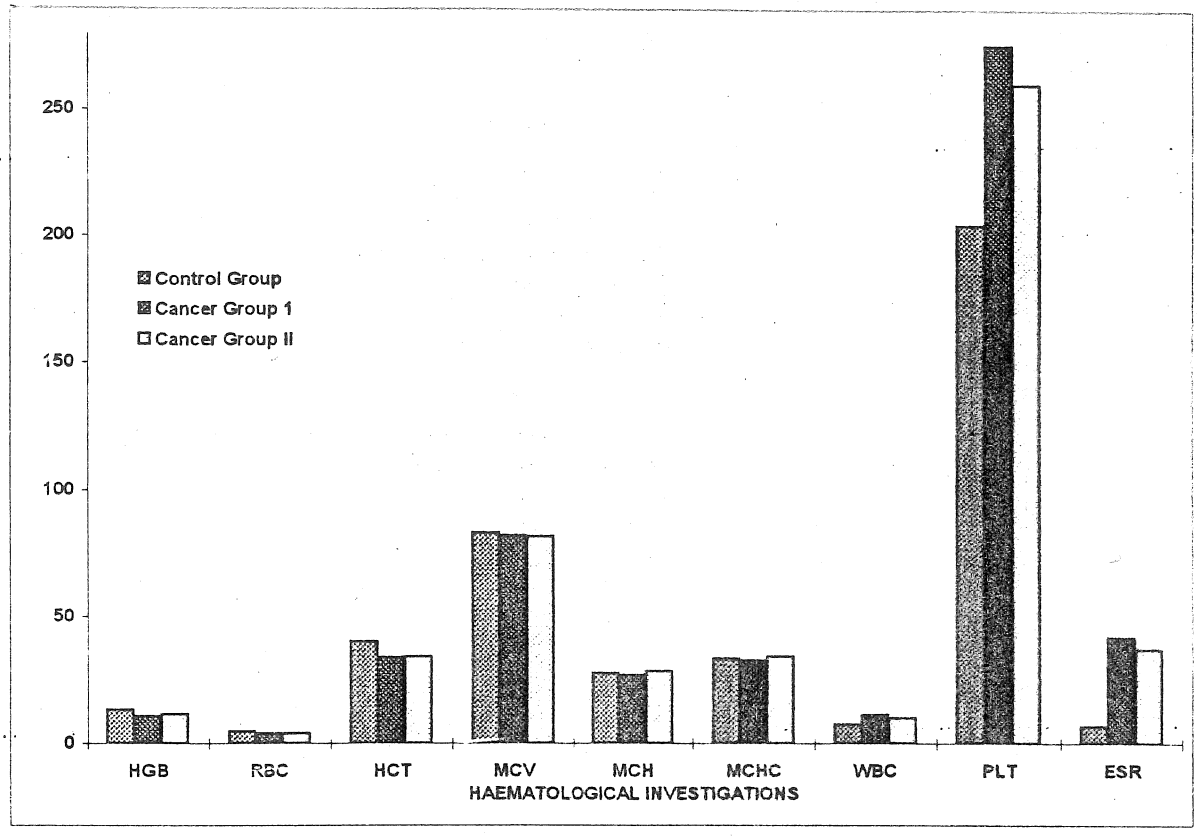

Figure. Haematological investigations in healthy control subjects vs patients of hepatocellular carcinoma before and after treatment

The control group value was compared with the respective normal value. The value of cancer group-I was compared with its respective control value and that of the cancer group-II with the respective value of cancer group-I,using Student's t Test(4).

The mean haemoglobin level was decreased to 10.85±1.83 g/dl ($P<0.01$). Kew et al. (7) studied 75 patients of HCC and 85% of them exhibited a low mean haemoglobin level of 11.2 g/dl and rest of them had haemoglobin within the normal range. Martin and Harold (14), in another study of 213 patients of HCC, observed that 73.7% had haemoglobin level within the range of 9-15 g/dl. The average erythrocyte count, in our study cases of HCC was observed to be 4.08±0.69 x 10^6/ µL ($P<0.01$), of which only 2% showed erythrocytosis while in another study erythrocytosis was demonstrated for 2.8% of HCC patients (14). Proliferation of liver in HCC might result in disturbances of hepatic metabolism which enhance the release of erythropoietin or diminish its inactivation (14). The mean haematocrit in our study was significantly decreased to 33.6±6.2% ($p<0.01$) as compared to control subjects. The decreased haemoglobin content, erythrocyte count and haematocrit ratio indicated the presence of anaemia in HCC. As the mean corpuscular volume was within the normal range, 81.93±4.06 fL ($P>0.05$), anaemia in HCC was normocytic and the reason might be chronic illness, haemolysis and haemoglobinopathy (12). There was a very singifi-

cant decrease in the mean corpuscular haemoglobin to 26.62±0.73 Pg (P<0.01), compared to the control subjects. The mean corpuscular haemoglobin concentration also decreased significantly to 32.41±1.61 g/dl (P<0.01). These were indicative of a very significant decrease in haemoglobin level as discussed above. Leukocyte and platelet counts were usually within the normal range as observed by other investigators(14). Only 6% of patients had leukocytosis that my be caused by an increase in one or more of the cell types that normally circulate in peripheral blood or by the presence of abnormal cell types (12). Erythrocyte sedimentation rate in patients with HCC was increased very significantly to 41.5±8.33 mm/1st hr (P<0.01). The vast majority of acute or chronic infections and most neoplastic and degenerative diseases are associated with changes in the plasme proteins (elevated plasme proteins, in particular fibrinogen, alpha and beta-globulins) which lead to an acceleration of sedimentation (9).

After 5,6 months of treatment there was a significant increase in haemoglobin contents, erythrocyte count, haematocrit ratio, mean corpucular haemoglobin and mean corpuscular haemoglobin concentration. While there was a slight decrease in mean corpuscular volume, leukocyte count, platelet count and erythrocyte sedimentation rate, our study revealed that chemotherapy had only a palliative effect in HCC. The data collected during the study also revealed that 81% of patients had undergone weight loss of varying degrees while Ihde et al (5), in another study, showed that 71.6% patients exhibited weight loss. The male to female ratio in HCC patients in our study cases was 11.5:1, similar to the findings of other authors who calculated a male to female ratio of 10.6:1(1). The age group which represented maximum patients of HCC was 60-70 years. The blood group "0" was prevalent for 36.70% in our study cases.

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