Original Article

A study of incidence and pattern of anaemia in patients with non-haematological malignancies

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Abstract

Introduction: Incidence of malignancies is on the rise. Advances in treatment protocols have resulted in increased longevity of the patients. Therefore greater focus is now on comorbid conditions, treatment of which would improve the survival and quality of life. **Aims and Objective:** To study the incidence and pattern of anaemia in patients with non-haematological malignancies. **Methodology:** This study was carried out in the department of Clinical Pathology on the patients admitted to an urban referral hospital. A total number of 40 in patients with various nonhaematological malignancies were screened for anaemia. Based on Hb cut-off of 12 g/dL, 33 of them were recruited for the study. Complete haemogram was done using Sysmex KX-21, fully automated haematology analyzer (manufacturers: Sysmex Corporation, Japan). **Result:** Out of the 33 peripheral smears studied, 70% (n=23) were normocytic normochromic, 21% (n= 7) were microcytic hypochromic, and the remaining 9% (n=3) were normocytic hypochromic; no evidence of bone marrow suppression or replacement was found. Seven out of eight men (87.5%) had reduced RBC count. Fifteen women (60%) had reduced RBC counts. All the men in the present study had reduced haematocrit. Twenty women (80%) had reduced haematocrit. Reduced MCV was observed in 10 patients (30.3%) out of 33 cases. Seventeen patients (51.5%) had reduced MCH. Eighteen patients (54.5%) had reduced MCHC. Fifteen patients (45.5%) had increased RDW. Ten patients (30%) had serum iron <50 µg/dL, 16 patients (48.5%) had serum ferritin >50 ng/mL, 13 patients (39.4%) had serum ferritin between 12–50 ng/mL and the remaining four patients (12.1%) had <12 ng/mL of ferritin. TIBC was within normal range in 18 patients (54.55%), low in 11 patients (33.33%), and raised in four patients (12.12%). **Conclusion:** Normocytic normochromic anaemia was most commonly seen. Red cell indices and serum iron, TIBC and serum ferritin were found to be useful parameters in precise assessment of anaemia and its type. Bone marrow suppression, haemolysis and abnormal renal / liver functions were not observed. This study proves that a number of different factors contribute to the development of anaemia in malignancy, and it is common for several factors to operate in patients with malignancy. The type of anaemia depends on the dominant underlying mechanism or mechanisms.

Keywords: Incidence and Pattern of Anaemia, Non-Haematological Malignancies.

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INTRODUCTION

Incidence of malignancies is on the rise. Advances in treatment protocols have resulted in increased longevity of the patients. Therefore greater focus is now on comorbid conditions, treatment of which would improve the survival and quality of life. Over the past decade, there has been a growing appreciation of anaemia as the source of a wide range of symptoms and poorer outcomes in cancer patients. Data published on 15 September, 2004 in the European Journal of Cancer[1] (online edition) reveals two out of three cancer patients suffer from anaemia and only 40% of these patients receive appropriate treatment (anaemia defined as haemoglobin less than 12 g/dL). Low haemoglobin levels correlate with poor quality of life and physical performance. Performance status deteriorates with decreasing haemoglobin. This correlation remains regardless of disease status or cancer treatment. J Jaime Caro *et al*[2], in their systematic and quantitative review of anaemia as an independent prognostic factor for survival in patients with cancer, found that anaemia was associated with shorter survival times for patients with lung carcinoma,

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cervicouterine carcinoma, head and neck cancer, prostatic carcinoma, lymphoma and multiple myeloma. The overall estimated increase in risk of death was 65% (54 – 77%). Tumour hypoxia may directly contribute to the resistance of the cancer patient to radiation therapy or chemotherapy via deprivation of the oxygen essential for the cytotoxic actions of these agents. Indirectly, tumour hypoxia may contribute to radioresistance and chemoresistance by inducing proteomic and genomic changes that lead ultimately to malignant progression, with reduced local control and metastatic spread, and ultimately, increased resistance and decreased survival time. A direct association between hypoxia and anaemia appears likely, and anaemia is a modifiable condition in many cancer patients. This being the case, reducing tumour hypoxia by correcting anaemia with recombinant human erythropoietin (rHuEPO) and other agents appears to offer one possible therapeutic option for enhancing the effectiveness of standard cancer therapies[3]. Hence, it is worthwhile to study the incidence and pattern of anaemia in cancer patients in our hospital and create a database so that timely intervention by the oncologists with strategies to improve the outcome of treatment can be instituted whenever anaemia is diagnosed.

MATERIAL AND METHODS

This study was carried out in the department of Clinical Pathology on the patients admitted to an urban referral hospital. Patients with non-haematological malignancies aged 19–69 years with Hb< 12 g/dL newly diagnosed, no prior chemo or radiotherapy and**,** no prior steroid administration were included into study while patients in relapse, patients on chemo or radiotherapy, prior surgery for the same and, systemic illnesses like cardiac, renal or hepatic disease (severe enough to affect haematopoisis) were excluded. A total number of 40 in patients with various nonhaematological malignancies were screened for anaemia. Based on Hb cut-off of 12 g/dL, 33 of them were recruited for the study. Since we receive about 1200 samples of nonhaematological malignancies in our department in a year, it represents about 2.75% of the incidence in our department. Complete haemogram was done using Sysmex KX-21, fully automated haematology analyzer (manufacturers: Sysmex Corporation, Japan).

RESULT

From **Fig.1** : Mild anaemia (Hb 10 – 12 g /dL) was present in 22 cases, moderate anaemia (Hb 8 – 9.9 g/dL) in 8 cases and severe anaemia (Hb<8 g/dL) in 3 cases (Fig-1).

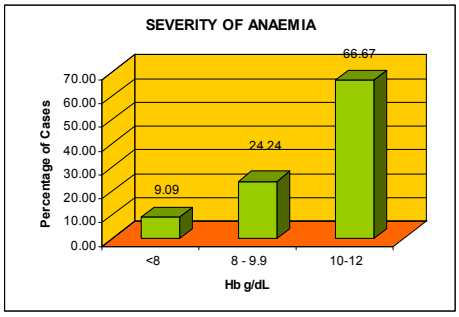

Figure 1

From **Fig 2:** Out of the 33 peripheral smears studied, 70% (n=23) were normocytic normochromic, 21% (n= 7) were microcytic hypochromic, and the remaining 9% (n=3) were normocytic hypochromic. No fragmented red cells or microspherocytes were noted in any of the smears (Fig-2).

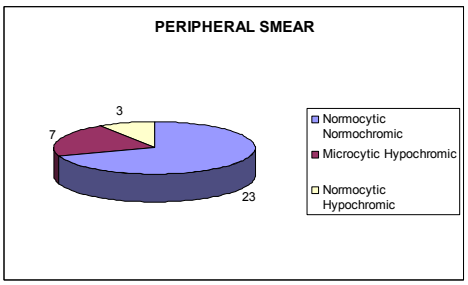

Figure 2

All patients had their total and differential WBC counts and platelet counts checked and their peripheral smears examined. No evidence of bone marrow suppression or replacement was found. All the 33 patients had normal liver and kidney function tests.

The haematological parameters observed

No of patients with Hb<12 g/Dl - 33, RBC count - 3.83 million / µL, Haemoglobin- 10.7 g/dL, Haematocrit- 34.4%, MCV - 84.9fL, MCH - 25.5 pg MCHC - 30.7 g/dL, Data are shown as Median.

Table 1: Hamatological parameters in Male and Female patients with Non-haematological malignancies

RBC million/µL Men	No.	Percent
< 4.5	7	87.5
4.5-5.9	1	12.5
RBC million/µLWomen	**No.**	**Percent**
< 4	15	60.0
4 – 5.2	10	40.0
Total	25	100.0
HCT %* Men	**No.**	**Percent**
< 40	8	100.0
HCT % Women	**No.**	**Percent**
< 36	20	80.0
36 – 46*	5	20.0
Total	**25**	**100.0**

From **Table 1:** Seven out of eight men (87.5%) had reduced RBC count. Fifteen women (60%) had reduced RBC counts. All the men in the present study had reduced haematocrit. Twenty women (80%) had reduced haematocrit.

Table 2: Various Haematological parameters in Patients with Non-Haematological Malignancies

MCV fL	No.	Percent
< 80	10	30.3
80 – 100	23	69.7
Total	33	100.0
MCH pg	**No.**	**Percent**
<26	17	51.5
26 – 34	16	48.5
Total	33	100.0
RDW fL	**No.**	**Percent**
39 – 46	18	54.5
> 46	15	45.5
Total	33	100.0
Serum Iron µg/dL	**No.**	**Percent**
< 50	10	30
50-150	23	70
Total	33	100.0
Serum ferritin ng/mL	**No.**	**Percent**
<12	4	12.1
12-50	13	39.4
>50	16	48.5
Total	33	100.0
TIBC µg/dL	**No.**	**Percent**
< 250	11	33.33
250 – 370	18	54.55
> 370	04	12.12
Total	**33**	**100.0**

From **Table 2:** Reduced MCV was observed in 10 patients (30.3%) out of 33 cases. Seventeen patients (51.5%) had reduced MCH. Eighteen patients (54.5%) had reduced MCHC. Fifteen patients (45.5%) had increased RDW. Ten patients (30%) had serum iron <50 µg/dL, 16 patients (48.5%) had serum ferritin >50 ng/mL, 13 patients (39.4%) had serum ferritin between 12–50 ng/mL and the remaining four patients (12.1%) had <12 ng/mL of ferritin. TIBC was within normal range in 18 patients (54.55%), low in 11 patients (33.33%), and raised in four patients (12.12%).

DISCUSSION

A survey of 38 studies, most of which evaluated anaemia prevalence in cancer patients before treatment found that the prevalence ranged from 5% (prostate cancer) to as high as 90% (multiple myeloma).The prevalence of anaemia appears to be especially high in patients with uterine-cervical cancers, advanced multiple myeloma and those suffering from cancer- related renal impairment[4]. In a study at Beth Israel Medical Center and St. Luke's-Roosevelt Hospital Center, USA, 48% of patients presented to the Radiation Oncology department with anaemia (Hb<12 g/dL) and a total of 57% ultimately became anaemic by the end of the therapy[5]. Data published in the European Journal of Cancer (online edition) dated 15th September 2004 reveals the following: (Anaemia defined as Hb<12 g/dL) Factors that contribute to anaemia in patients with nonhaematological malignancy[6,7] : blood loss, infections and 'inflammatory – like' response. Less common factors: bone marrow infiltration, inadequate nutrition, impaired renal function, haemolysis and myelosuppressive effects of treatment[8] The anaemia of chronic disease presents itself as a normochromic normocytic anaemia[9]. It normally does not lead to a decrease in haemoglobin below 8 g/dL. The diagnosis is usually established by a low serum iron concentration, a low transferrin concentration, a low transferrin saturation, and normal or increased ferritin values in the presence of a chronic illness[10,11]. The number of reticulocytes is usually low, which points to a small rate in de novo production. Serum values of iron and transferrin saturation are normally reduced, because the iron is trapped inside the reticuloendothelial system[12] In Our study we have found among anaemic patients, 66.67% had mild anaemia, 24.24% had moderate and another 9.09% had severe anaemia. The pattern and severity of anaemia generally reflects that of the European Cancer Anaemia Study (ECAS). Proportion of patients with moderately severe anaemia was a little less when compared to ECAS. In the present study, mean Hb, RBC count, Haematocrit, MCV, MCH and MCHC were lower in men and these values varied more widely in men. Mean RDW was higher in men and RDW varied more widely in men. Mean serum iron and mean serum ferritin were higher in women and mean TIBC was lower in women. These findings indicate that iron deficiency predominates over other factors in the causation of anaemia in male cancer patients in the present study. Mean Haemoglobin, RBC count, Haematocrit, and MCV were the lowest in above 60 years age group. Mean RDW was the highest in above 60 years age group. Mean MCH, MCHC and mean serum iron were the lowest in 40 years or below age group. In the present study, 12 patients had both reduced MCH and reduced MCHC. Among them only six patients had reduced serum iron. This is explained by the fact that the red cell indices are mainly helpful in detecting mild or early red cell abnormalities. In severe anaemias, peripheral blood smear is sufficiently characteristic and red cell indices do not provide additional information. 17 patients had serum ferritin levels <50 ng/mL. Among them eight patients had both MCH and MCHC reduced, six patients had either MCH or MCHC reduced and the remaining three had both

MCH and MCHC in the normal range. In the present study of cancer patients with anaemia, RBC counts were within the normal range in 11 patients. The red cell count can be in the normal range in people who are anaemic on the basis of the haemoglobin level when the red cells are microcytic, as in thalassemia minor or iron deficiency[13]. In the present study, six patients had reduced MCV and increased RDW indicating iron deficiency. Among these patients three had serum ferritin levels less than 12 ng/mL, two had serum ferritin between 12 and 50 ng/mL and one patient had ferritin level more than 50 ng/mL. Haematocrit was within normal range in five women. All of them had mild anaemia, normal red cell count and normal serum iron. Among them, in only one patient, MCV, MCH and MCHC were within the normal range. The others had at least one parameter reduced. This again proves the utility of red cell parameters as indicators of early or mild red cell change. Out of the seven microcytic hypochromic peripheral smears, six were accounted for by carcinoma of oesophagus and stomach and the remaining one by carcinoma of breast. In the present study, out of the eleven cases of carcinoma of breast, nine had normocytic normochromic, one had normocytic normochromic to hypochromic and the other had microcytic hypochromic peripheral smears. Ten patients had reduced MCV. While seven of them had microcytic hypochromic peripheral smears, other smears also had microcytic hypochromic red cells in varying proportions. In the present study 17 patients had reduced MCH. Among them, only seven peripheral smears were microcytic hypochromic and three others were normocytic normochromic to hypochromic. The remaining seven smears were predominantly normocytic normochromic but also had hypochromic microcytic red cells in varying proportions. This proves that red cell indices are mainly helpful in detecting mild or early red cell abnormalities and peripheral smear is sufficiently characteristic in severe anaemias. The peripheral smear picture correlated well with serum ferritin levels in the present study. Four patients had serum ferritin levels < 12 ng/mL, all of them had microcytic hypochromic peripheral smear. In the present study, 17 patients had serum ferritin < 50 ng / mL indicating most probable iron deficiency. Among them, 11 patients had normocytic normochromic, five had microcytic hypochromic and the remaining one had normocytic hypochromic peripheral smears. Out of the three patients with Hb<8g/dL, two had microcytic hypochromic smears while the other had mainly normocytic normochromic picture with many microcytic hypochromic red cells. Out of the seven patients with microcytic hypochromic peripheral smears, only two had reduced serum iron levels. The remaining five patients had serum iron levels between 50 and 70/ µg/dL.

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