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## ORIGINAL ARTICLE

# PATTERN OF ANAEMIA AMONG NON-HAEMATOLOGICAL MALIGNANT PATIENTS IN A TERTIARY CARE HOSPITAL: A CROSS-SECTIONAL STUDY

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**Abstract:**

***Background:*** *Anaemia is a frequent complication in cancer patients and has been linked to a reduction in quality of life as well as a poor prognosis. Considering the paucity of dataregarding anaemia in non-haematological carcinoma in developing countries, this studyaimed to evaluate the pattern of anaemia in non-haematological carcinoma patients admitted in a tertiary care hospital of Bangladesh.* ***Methods:*** *This cross-sectional study was conducted over 56 adult anaemic patients of non-haematological carcinoma inDhaka Medical College Hospital, from 1st of September 2017 to 1stdecember 2017.After getting written informed consent, a detailed history, clinical examination and thorough investigation were carried out in each patient. All the methods in the present study were carried out following the ethical guidelines of the 1975 Declaration of Helsinki.Data were recorded in separated case record form and analyzed by IBM SPSS version 26.* ***Results:*** *The majority of the study participants were male (62.5%), aged >50 years (64.3%), and from rural areas (60.7%). Metastasis affected 50% of the research participants, and colorectal carcinoma (17.9%) was the most common type of non-haematological carcinoma. The majority of patients had moderate to severe (73.2%), hypochromic (62.5%), and microcytic (62.5%) anemia. In contrast to patients without colorectal cancer, those who had it were more likely to get severe anemia (p=0.001). In patients with metastasis, the likelihood of having hemoglobin below 10 g/dL was 11.27 times higher than in patients without metastasis (COR = 11.27; 95% CI 2.23-56.86).* ***Conclusion:*** *Maximum anaemic non-haematogical patients had haemoglobin <10 g/dL with microcytosis and hypochromia.*

***Keywords:*** *Non-haematological carcinoma, Solid malignancy, Anaemia*

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**Introduction:**

Anemia is a clinical status indicated by a reduced red blood cell (RBC) mass together with low hemoglobin (HGB) and hematocrit levels.[1] Anemia is a critical issue for cancer patients since it has been linked to worse medical outcomes[2] and may worsen their already compromised health.[3] Anemia is expected to affect 30% to 90% of cancer patients at some point during their treatment.[4–6]The occurrence of cancer-related anemia varies according to the nature, stage, duration and spread of the malignancy, as well as the type and timing of therapy.[7] In a meta-analysis, anemic patients with lung cancer, cervico-uterine carcinoma, head and neck cancer, prostate cancer had shorter survival times than those without anaemia.[8] It is an indicator of poor prognosis in T1-T2 squamous cell carcinoma of the glottic larynx.[9]

As Malignancy results by uncontrolled division of cells and the ability of these cells to invade other tissues, either directly or by metastasis, therefore, different types of cancers present differently and in diversified manner.[10] An abnormal hematological picture may be the first manifestation of many non-hematological malignancies.[11] In addition, anaemia is a recognized complication of myelosuppressive chemotherapy, and it has been estimated that around 1.3 million cancer patients who are not anemic at the time of diagnosis may acquire anaemia during the course of their disease in the United States.[12] Most studies have found that pre-treatment anaemia is an important predictor of prognosis, survival, and disease free period.[13]Grigieneet al. and Zhang et al., in their study found that the hemoglobin (Hb) level before treatment had a significant influence on overall survival, disease-free survival and local relapse-free survival in uterine cervical carcinoma treated with irradiation[14] and Breast Cancer[13], respectively.

The cause of anaemia in cancer patients is diverse and frequently complicated. It may be the result of malignancy itself, acute or chronic blood loss, hemolysis, marrow suppression from medication, or chronic illness anaemia.[15] Besides, iron metabolism disorders, bone marrow insufficiency or infiltration, malnutrition, tumor catabolism, and erythropoietin deficiency also play key role in anemic pathogenesis.[11] In addition, interaction of immune system with iron metabolism and erythropoiesis is known to be an important factor in the development of anaemia in cancer patients.[16]

On the whole, cancer-associated anemia confers general adverse consequence mainly in anemic patients with lung, prostate, or head and neck cancers or lymphoma, which have a substantial decrease in survival time compared to their nonanemic counterparts.[7] Therefore, It is essential to recognize the incidence and severity of anemia among cancer patients to support the most appropriate treatment plans. Several studies have undergone to examine the relation of anaemia with hematological malignancies. However, study regarding anaemia or hematological presentation of non-haematological malignancies are scarce, and hence, this study was designed to evaluate the pattern of anaemia in non-haematological malignancy patients admitted in a tertiary care hospital of Bangladesh.

**Methodology:**

*Study design, settings and sample:*

This descriptive cross-sectional study was conducted in the departments of medicine, surgery and oncology in Dhaka Medical College Hospital, a tertiary care center of Bangladesh. The study data were collected between 1st Sept 2017 to 1st December 2017.Based on the number of patients admitted per month, an estimated participation rate of 50%, and the time allocated for data collection, we finally recruited a convenience sample of 56 adult anaemic patients from aforementioned departments of the study site, who were admitted due to any type of non-haematological carcinoma. Patients who were severely ill and having other associated diseases responsible for anaemia, were excluded from this study.

**Data collection procedure:**

After admission of an anaemic patient with non-haematological carcinoma in the hospital ward, the case was immediately assessed by the indoor medical officer and the principal investigator (PI) was informed. The PI then immediately examined the patient thoroughly. After fulfilling the inclusion and exclusion criteria, each patient was enrolled with unique ID. Patient's guardians were briefed about the objectives of the study, benefits, freedom for participating in the study and confidentiality. Informed written consent was obtained from each patient and/or their guardian. Face to face interview was conducted by using a semi-structured questionnaire. Data were collected at enrollment including age, gender, residence, family history of carcinoma, history of tobacco and alcohol consumption. Venous blood samples were obtained

from the patients on admission and measurements of blood counts (red blood cell, haemoglobin, haematocrit, and red blood cell indices) were performed immediately after sampling. All the collected data were recorded in a separate case record form.

**Operational definition:**

Anaemia was defined as an Hb level <12 g/dL, in accordance with the toxicity grading criteria from the National Cancer Institute and the European Organization for Research and Treatment of Cancer. For statistical analyses, anaemia was further categorized as: Mild anaemia: Hb 10 - 12.9 g/dl for men & Hb 10 - 11.9 g/dl for women; Moderate anaemia: Hb 7 - 9.9 g/dl for both genders and severe anaemia: Hb < 7 g/dl for both genders.

**Data acquisition and statistical Analysis:**

Following data collection, entered into a password-protected Microsoft Access data entry platform. The entered data were assessed for completeness, accuracy and consistency before analysis was commenced. Data analysis was carried out by using SPSS version 26 (IBM Corp., Armonk, NY). Continuous data were expressed as mean and standard deviation. Categorical data were expressed as frequency and percentage. To determine the association between categorical variables, chi square test was done. Mean comparisons were assessed by student t-test. Univariate logistic regression to detect factors associated with moderate to severe (haemoglobin<10 g/dL) anaemia. Statistical significance was set at p <0.05, with a 95% confidence interval.

**Result:**

Maximum study patients were male (62.5%), aged >50 years (64.3%), and hailed from rural residence (60.7%). History of tobacco and alcohol consumption were given by 44.6% and 10.7% patients, accordingly. Family history of any type of carcinoma was present in 21.4% patients. In this study, colorectal carcinoma (17.9%) was the most common type of non-haematological carcinoma followed in decreasing order lung carcinoma (16.1%), upper GI carcinoma (12.5%), gynaecological carcinoma (12.5%), hepatobiliary carcinoma (8.9%) and miscellaneous type of carcinoma (21.4%). Half of the study patients had metastasis (50%). [Table I].

In this study, maximum patients had microcytic (62.5%), hypochromic (62.5%) and moderate to severe (73.2%) anaemia. [Figure 1]

**Table-I**

*Socio-demographic profile of study participants (N=56)*

| Variables | n (%) |
|---|---|
| Gender | |
| Male | 35 (62.5) |
| Female | 21 (37.5) |
| Age (in years) | |
| 21-30 | 8 (14.3) |
| 31-40 | 4 (7.1) |
| 41-50 | 8 (14.3) |
| 51-60 | 12 (21.4) |
| 61-70 | 16 (28.6) |
| >70 | 8 (14.3) |
| Residence | |
| Rural | 34 (60.7) |
| Urban | 22 (39.3) |
| Occupation | |
| Government employee | 4 (7.1) |
| Non-government employee | 13 (23.2) |
| Business | 8 (14.3) |
| House wife | 12 (21.4) |
| Unemployed | 7 (12.5) |
| Others | 12 (21.4) |
| History of tobacco consumption | 25 (44.6) |
| History of alcohol consumption | 6 (10.7) |
| Family history of cancer | 12 (21.4) |
| Tumourlocation | |
| Breast | 6 (10.7) |
| Lung | 9 (16.1) |
| Colorectal | 10 (17.9) |
| Upper GI | 7 (12.5) |
| Gynaecological | 7 (12.5) |
| Hepato-billiary | 5 (8.9) |
| Others | 12 (21.4) |
| Presence of metastasis | 28 (50) |

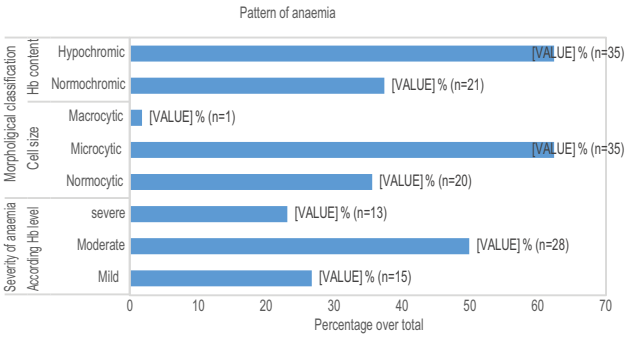


**Fig.-1:** *Pattern of anaemia in non-haematological malignant patients (N=56)*

Patients with colorectal carcinoma suffered more severe anemia as compared to a patient without colorectal carcinoma (p=0.001). Besides, patients with metastasis had significant association with severity of anaemia (p=0.003). Nevertheless, there was no statistically significant difference found in gender, age group, residence, family history of carcinoma, tobacco and alcohol consumption among the severity of anemia. [Table II]

Univariate logistic regression analysis showed that patients with metastasis were 11.27 times more likely to have haemoglobin <10 g/dL than those without metastasis (COR = 11.27; 95% CI 2.23–56.86). [Table III]

**Table II**

*Haemoglobin level and severity of anaemia according to different socio-demographic factors. (N=56)*

| | Haemoglobin level | | | Severity of anaemia | | | |
|---|---|---|---|---|---|---|---|
| | Minimum to maximum | Mean±SD | $P_1$ | Mild n (%) | n (%) Moderate | n (%) Severe | $P_2$ |
| All (n=56) | 3.90-12.30 | 8.59±1.92 | | 15 (26.8) | 28 (50.0) | 13 (23.2) | |
| **Gender** | | | 0.239 | | | | 0.464 |
| Male | 3.90-12.30 | 8.34±2.10 | | 9 (25.7) | 16 (45.7) | 10 (28.6) | |
| Female | 5.50-10.90 | 8.99±1.53 | | 6 (28.6) | 12 (57.1) | 3 (14.3) | |
| **Age (in years)** | | | 0.402 | | | | 0.184 |
| 21-50 | 3.90-11.20 | 8.19±2.18 | | 6 (30.0) | 7 (35.0) | 7 (35.0) | |
| >50 | 4.50-12.30 | 8.81±1.75 | | 9 (25.0) | 21 (58.3) | 6 (16.7) | |
| **Residence** | | | 0.987 | | | | 0.241 |
| Rural | 4.50-12.30 | 8.67±1.77 | | 8 (23.5) | 20 (58.8) | 6 (17.6) | |
| Urban | 3.90—11.20 | 8.47±2.16 | | 7 (31.8) | 8 (36.4) | 7 (31.8) | |
| **History of tobacco consumption** | 3.90-12.30 | 8.33±2.16 | 0.448 | 7 (28.0) | 10 (40.0) | 8 (32.0) | 0.297 |
| **History of alcohol consumption** | 7.28-10.30 | 9.26±1.16 | 0.414 | 3 (50.0) | 3 (50.0) | 0 (0.0) | 0.233 |
| **Family history of cancer** | 5.42-10.90 | 7.94±1.74 | 0.165 | 2 (16.7) | 6 (50.0) | 4 (33.3) | 0.584 |
| **Tumour location** | | | | | | | |
| Breast | 8.90-10.90 | 9.65±0.72 | 0.245 | 1 (16.7) | 5 (83.3) | 0 (0.0) | 0.191 |
| Lung | 6.90-11.00 | 9.21±1.24 | 0.396 | 3 (33.3) | 5 (55.6) | 1 (11.1) | 0.633 |
| Colorectal | 3.90-11.20 | 6.78±2.25 | 0.006 | 1 (10.0) | 2 (20.0) | 7 (70.0) | 0.001 |
| Upper GI | 6.10-12.30 | 8.21±2.12 | 0.329 | 1 (14.3) | 4 (57.1) | 2 (28.6) | 0.724 |
| Gynaeological | 5.00-10.30 | 8.45±1.76 | 0.734 | 1 (14.3) | 5 (71.4) | 1 (14.3) | 0.478 |
| Hepato-billiary | 5.50-10.10 | 8.42±1.99 | 0.933 | 2 (40.0) | 2 (40.0) | 1 (20.0) | 0.782 |
| Others | 5.00-10.90 | 9.48±1.56 | 0.058 | 6 (50.0) | 5 (41.7) | 1 (8.3) | 0.093 |
| Presence of metastasis | 4.50-10.90 | 8.13±1.71 | 0.016 | 2 (7.1) | 19 (67.9) | 7 (25.0) | 0.003 |

SD=standard deviation, GI= Gastro-intestinal.$P_1$was determined by independent sample T test and $P_2$was determined by Chi-square test.

**Table III**

*Univariate logistic regression to detect factors associated with moderate to severe (haemoglobin<10 g/dL) anaemia (N=56)*

| Factors | 95%CI (lower-upper) | p-value |
|---|---|---|
| Male gender | 1.16 (0.344-3.89) | 0.815 |
| Age >50 years | 1.29 (0.38-4.35) | 0.686 |
| Rural residence | 1.517 (0.458-5.02) | 0.495 |
| Having history of tobacco consumption | 0.894 (0.273-2.93) | 0.854 |
| Having history of alcohol consumption | 0.316 (0.056-1.78) | 0.191 |
| Having family history of cancer | 1.74 (0.312-9.69) | 0.528 |
| **Tumour location** | | |
| Breast | 1.94 (0.208-18.16) | 0.560 |
| Lung | 0.686 (0.148-3.18) | 0.630 |
| Colorectal | 3.94 (0.454-34.12) | 0.213 |
| Upper GI | 2.40 (0.264-21.79) | 0.437 |
| Gynaeological | 2.40 (0.264-21.79) | 0.437 |
| Hepato-billiary | 0.513 (0.077-3.42) | 0.491 |
| Others | 0.257 (0.067-1.01) | 0.058 |
| **Presence of metastasis** | 11.27 (2.23-56.86) | 0.003 |

OR=odds ratio, CI= confidence interval, GI=Gastro-intestinal

**Discussion:**

Anemia in cancer patients is a consequence ofmalignancy itself, anti-cancer treatment, blood losses, nutritional deficiencies, hemolysis, endocrine disorders, or inflammatory cytokines associated with chronic diseases. In the present study, 56 anaemic non-haematological carcinoma patients at Dhaka Medical College Hospital of Bangladesh, were assessed for pattern of anemia. This study found thatmajority study patients had moderate to severe anaemia (Hb <10 g/dL). This might be because of bone marrow suppression from chemotherapy, radiation therapy and bone metastases due to the breast, lung, kidney, bladder and prostate cancer. About half of the patients had metastasis in this study, and metastasis was found to be the significant risk factor for developing moderate to severe anaemia in non-haematological carcinoma (unadjusted odds ratio = 11.27; 95% CI 2.23–56.86). Similarly, several previous studies also observed the association between metastasis and anaemia in different non-haematological cancers.[17–19] Moreover, some studies also reported that microangiopathic hemolytic anemia (MAHA) is a presenting feature of an occult malignancywith documented metastases.[20,21] Hence, prompt diagnosis is essential because conditions that mimic the symptoms of MAHA, including thrombotic thrombocytopenic purpura, have different prognoses and therapeutic options.[18]

In present study, maximum non-haematological carcinoma patients had microcytic and hypochromic anaemia.Our findings corresponds to the study done by various other authors on different non-haematological carcinoma.[22,23] In addition,a cohort study of patients aged e 40 years using UK primary care electronic patient records found that microcytosis is a predictor of underlying cancer, especially in colorectal, lung, breast, kidney and stomach carcinoma. However, in contrast to our study findings, several studies found normocytic normochromic anaemia is the most prevalent type in non-haematogical carcinoma patients,[11,23] which might be due to the variation in cancer types, disease stage, and treatment modalities.

In current study, colorectal carcinoma (17.9%) was the most frequent non-haematological carcinoma followed in decreasing order lung carcinoma (16.1%), upper GI carcinoma (12.5%), gynaecological carcinoma (12.5%), hepatobiliary carcinoma (8.9%) and miscellaneous type of carcinoma (21.4%). Previous studies also found lung carcinoma and colorectal

carcinoma as the commonest non-haematological carcinoma.[7,24] Moreover, this study observed that patients with colorectal carcinoma hadhigher frequency of severe anemia as compared to a patient without colorectal carcinoma (p=0.001). This confirms the results of several previous studies.[25,26] One of the main causes of anemia in colorectal carcinoma patients is blood loss to the bowel leading to iron deficiency.[27,28] Indeed, anemia in CRC has been reported to frequently show microcytic phenotype[25], which also support our study findings.

In this study, maximum study patients were older aged, male and hailed from rural residence. This is probably because of the fact that the elderly people often present in hospitals in very late stages of their disease conditions in our country. Besides, rural people often have a bad habit of heavy smoking of low-grade nicotine cigarettes and hookahs, and they also have to use non-electric makeshift ovens that let out a lot of smoke while cooking causing COPD changes in them. As they age, they often present with lung disease conditions.Our study found no significant association of age and gender with severity of anaemia. This finding is similar to a study done in Ethiopia showing that gender and age category did not show any evidence of association with severity of anemia among patients with solid malignancy.[24]

Our results may not be generalizable due to a number of limitations. First off, the sample size was small, thus there weren't enough cases of each form of tumor. Secondly, both new and old cases were considered that might have an impact on the overall anaemia pattern. Thirdly, we did not specially track treatment effect in study subject that might affect the study result. Fourth, shortage of accompanying iron studies and evaluation of other factors that can affect iron indices could not be evaluated.

**Conclusion:**

The majority of the anemic non-haematological patients in this study showed microcytosis and hypochromia in addition to hemoglobin levels below 10 g/dL. Patients with colorectal cancer and metastatic disease were more likely to experience moderate to severe anemia. However, we advise conducting more, larger studies to examine the effect of anemia on non-haematological cancer and treatment outcomes.

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**Conflict of Interests:** None

**Ethical consideration:** Ethical measures were taken throughout the study period to maintain a high standard of confidentiality and anonymity of the participants. Formal approval was taken from the ethical review committee of Dhaka Medical College Hospital.

**Consent for Publication:** The authors agreed to publish the article by written consent.

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