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Original Research Article

Study of anemia in non-luminal solid tumors

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ABSTRACT

Background: Anemia is particularly prevalent in India due to widespread malnutrition. Cancer related anemia affects about three-fourths of cancer patients, causing symptoms like fatigue, appetite loss, and difficulty concentrating, and can worsen cancer prognosis, lengthen treatment, and reduce survival rates. Anemia is a significant cause of tumor hypoxia, which exacerbates the side effects of radiotherapy and chemotherapy, and affects energy levels and emotional distress.
Methods: The present cross-sectional study aims to assess the prevalence and types of anemia in patients with newly diagnosed non-luminal solid tumors. The study sample included all patients meeting the inclusion criteria, with a sample size of 100. Clinical evaluation and investigations were carried out to determine the presence and severity of anemia. Data was compiled and analyzed.
Results: Of the 100 patients enrolled, 68% had evidence of anemia, and the majority of them were in the age group of 51-60 years. Anemia's association with body mass index (BMI) was noted and was more common in underweight and normal-weight patients. The commonest malignancies in the study were head and neck cancers, breast cancers and female genital cancers, and the incidence of anemia in these malignancies was higher than in other tumors. When sub-classified a higher prevalence in gynecological tumors was noted. The majority of anemic patients had mild anemia, with microcytic hypochromic anemia being the most common type.
Conclusions: The study provides valuable information on the incidence and severity of anemia in patients with non-luminal solid tumors, which can help clinicians in their treatment planning and management.

Keywords: Anemia, Solid tumors, Cancer

INTRODUCTION

Anemia is a condition that develops when there are insufficient healthy red blood cells that can be characterized either by low hemoglobin, red blood cell (RBC) or hematocrit values.[1,2]

According to National Comprehensive Cancer Network (NCCN) recommendations, anemia is defined as hemoglobin levels that are less than 11 g/dl or ≥2 g/dl below the baseline.[3,4] Cancer frequently results in anemia, and cancer is one of the chronic diseases most frequently linked to anemia.[3]

Cancer-related anemia (CRA) is a significant healthcare issue as during their illness, anemia affects about three-fourths of cancer patients, which lowers their quality of life by causing symptoms like fatigue, lethargy, appetite loss, and difficulty concentrating.[4]

Anemia affects a large percentage of cancer patients, with 13% of cancer patients who were not anemic at the time of diagnosis developing it. The likelihood of developing cancer-related anemia (CRA) varies according to the kind of cancer, its stage, how long it has been present, the intensity and type of tumor therapy regimen employed, the presence of concurrent infections or surgery, and many

other factors.[4] By worsening the prognosis of cancer, lengthening the course of treatment, and lowering the survival rate, it is also one of the main causes of morbidity in cancer patients.[5]

Cancer-related or non-related causes can both contribute to anemia in cancer patients. The underlying comorbidities (such as bleeding, hemolysis, nutritional deficiencies, and hemoglobinopathies) or infections are examples of non-cancer-related etiologies.[1] In cancers, anemia may result from either a tumor's direct effects or a treatment's side effects. Through the infiltration of bone marrow by solid tumors, which suppresses hematopoiesis, or by activating the immune system, which results in the production of cytokines like IL1, interferon-y, IL6, and TNF-α, which may be able to reduce hemoglobin levels through hemolysis, suppress erythropoiesis, prevent the release and synthesis of endogenous erythropoietin, or lessen the response of. [6,7]

Anemia or pancytopenia may be signs of myelophthisis, which happens when solid tumors replace the bone marrow in the body.[1] Tumor hemorrhage can cause blood loss (for example, in cases of hepatoma, gastrointestinal, bladder, and gynecologic tumors), and organ damage can make cancer-related anemia worse.[8,9]

Anemia is a significant cause of tumor hypoxia, which lengthens the course of treatment, and reduces the likelihood of survival. In addition to causing emotional distress, anemia also affects energy levels (fatigue).[10]

As a result, we conducted the current study to determine the prevalence of anemia and related factors among newly diagnosed patients with solid malignancy at a tertiary care facility.

METHODS

The study was a cross-sectional observational study conducted at Bharati Hospital and Research Center, Pune, India over a period of two years from October 2020 to October 2022. The study population consisted of treatment-naïve patients with non-luminal solid tumors, and the study sample included all patients who met the inclusion criteria. The sample size was determined to be 90 based on the prevalence and SD (p=58.4).[11]

Inclusion criteria

All consenting adults with treatment naïve patients with biopsy proven non-luminal solid malignancy.

Exclusion criteria

Patients with sepsis, disseminated intravascular coagulopathy, pre-existing chronic kidney disease, chronic alcoholic patients, known case of malabsorption syndrome, and patients on any medication that are known to cause anemias.

The study was approved by institutional ethics committee. After obtaining written consent, clinical evaluation of the patients was carried out along with general and systemic investigations, including hemogram to determine anemia status.

Relevant investigations like hemogram were performed and by assessing the hemoglobin value the patient was classified as anemic or non-anemic (according to WHO (accessed 05 September 2017), normal Hb values are ≥12 g/dl in women, and ≥13g/dl in men. The NCI grading of anemia is defined as follows: “mild (grade 1), Hb from 10 g/dl to the lower normal limit; moderate (grade 2), Hb 8.0–9.9 g/dl; severe (grade 3), Hb <8 g/dl to 6.5 g/dl; life-threatening (grade 4), Hb <6.5 g/dl”). The anemic patients were further tested to determine the type pf anemia (microcytic, macrocytic, normocytic) and possible etiology (iron deficiency and B12 deficiency).

The data was analyzed using statistical package for social sciences (SPSS) version 26.0 software. Continuous variable was presented as descriptive statistics and categorical variable results were presented as frequency and percentages. Group comparisons of categorical variables was done using Chi square test like severity and outcome categories. Student ‘t’ test was used for continuous variables with normal distribution. All results shown with 95% of confidence interval and p value of <0.05 were considered as significant.

RESULTS

Total of 100 patients with non-luminal tumors from tertiary care teaching hospital were recruited in the study. Among 100 enrolled patients with non-luminal solid tumors, 56 were females and 44 were males. From the screened patients, maximum population was found to be in the age group of 51-60 years, with the mean age of the patients was 54.76±12.46 years ranging between 19 to 82 years. Out of 100 non-luminal tumor patients 68% had evidence of anemia, as per WHO standard. There were more females (41) with anemia than males (27) and more males (17) without anemia than females (15). Table 1 shows that there is no statistically significant association between anemia status and gender (p=0.21). A statistically significant association between anemia status and BMI category (p=0.027) is reported. The number of individuals with anemia was highest with normal BMI category (39), followed by the overweight (15) category.

Table 2 shows the distribution of anemia in various types of cancer. The results suggest that there is no statistically significant association between anemia and the different types of cancer examined (p=0.38). Specifically, the highest number of individuals with anemia was observed in the head and neck cancer group (16), followed by CA breast (17), and female genital cancers (12). For some cancer types, there were no individuals with anemia, including hepatocellular carcinoma and phyllodes tumor. Even though, the association between various

malignancies and presence/absence of anemia was not found to be statistically significant, it was observed that when sub-classified into gynecological and non-gynecological tumors, significant association was found (p value=0.03). Specifically, among the types of malignancies, gynecological malignancies had a higher prevalence of anemia (30 individuals with anemia out of 37 total) compared to non-gynecological malignancies (38 individuals with anemia out of 63 total), as showed in Table 3.

Regarding RBC morphology, the highest number of individuals with anemia was observed in the microcytic hypochromic group (38 individuals with anemia out of 38 total), followed by the Normocytic normochromic group (24 individuals with anemia out of 56 total). Additionally, the macrocytic anemia group had a smaller number of individuals with anemia (6 individuals with anemia out of 6 total) (Table 4).

The anemia in patients with non-luminal tumors was divided into grades as mild, moderate and severe categories as per NCI grading. Out of 68 patients with anemia, maximum number of patients had mild anemia which was 44 (64.7%) while moderate and severe anemia was found in 17 (25%) and 7 (10.3%) respectively. Table 5 indicate that there is a statistically significant association between the category of grade of anemia and type of anemia (p=0.007).

Table 1: Association of presence of anemia with gender and BMI.

Category	Anemia		Total	Chi square value	P value
	Yes	No			
Gender				1.59	0.21
Female	41	15	56		
Male	27	17	44		
BMI					
Underweight	14	5	19	2.64	0.027*
Normal	39	15	54		
Overweight	15	12	27		

Table 2: Association between category of malignancy and presence or absence of anemia.

Parameters	Anemia		Total	Chi square value	P value
	Yes	No			
Head and neck cancer	16	13	29	10.69	0.38
CA breast	17	5	22		
Female genital cancers	12	2	14		
CA lung	6	6	12		
CA prostate	8	3	11		
CA pancreas	3	2	5		
CA gall bladder	3	1	4		
CA bladder	1	0	1		
Hepatocellular carcinoma	1	0	1		
Phyllodes tumor	1	0	1		

Table 3: Association between gynecological/non-gynecological malignancies and presence/absence of anemia.

Category	Anemia		Total	Chi square value	P value
	Yes	No			
Gynecological	30	7	37	4.61	0.03
Non-gynecological malignancies	38	25	63		

Table 4: Association between gynecological/ non gynecological malignancies, RBC morphology and presence/ absence of anemia.

RBC morphology	Anemia		Total	Chi square value	P value
	Yes	No			
Macrocytic anemia-megaloblastic	6	0	6	36.97	<0.001*
Microcytic hypochromic- iron deficient	38	0	38		
Normocytic normochromic-anemia of chronic disease	24	32	56		

Table 5: Association between category of grade of anemia and type of anemia.

Category	Anemia of chronic disease	Iron deficiency anemia	Vitamin B12 deficiency megaloblastic anemia	Total	Chi-square value	P value
Mild	23	19	2	44	14.08	0.007*
Moderate	2	12	3	17		
Severe	0	6	1	7		
Total	25	37	6	68		

DISCUSSION

Cancer-related anaemia (CRA) and fatigue are common side effects of cancer, negatively affecting patients' quality of life and prognosis.[12,13] Mild to moderate anaemia was not prioritized in cancer management until recently.[14,15] Anemia is frequently identified in advanced-stage cancer patients and can occur due to chronic inflammation caused by cancer even without antineoplastic treatment.[16] Studies have shown that anemia increases mortality risk and complications such as pulmonary edema. It has been found in 30-90% of cancer patients, depending on the type of cancer.[17,18]

The present study aimed to evaluate the prevalence and severity of anemia in patients with non-luminal solid tumors. A total of 100 patients were recruited from a tertiary care teaching hospital, with a higher proportion of females (56%) than males (44%). The majority of patients were in the age group of 51-60 years, with a mean age of 54.76±12.46 years. A significant association was observed between anemia status and BMI category, with the highest number of individuals with anemia in the normal BMI category. Our study found that there was no statistically significant correlation between age and gender distribution of patients and the prevalence of anemia. However, Muthanna et al reported that older patients had a higher incidence of anemia.[12]

In this study, the results are quite concerning, as a staggering 68 percent of the 100 patients with non-luminal tumours reported experiencing anaemia. On average, the haemoglobin levels of these anaemic patients were measured at 11.24, which is below the normal range, indicating a significant health concern. Further analysis revealed that the majority of these patients were suffering from iron deficiency anaemia, which is a particularly debilitating form of anaemia.

The majority of patients in Kifle et al's study were female (66%) and belonged to the 35-49 age group (36%).[8] Xu et al reported a high prevalence rate of 89.5% among cancer patients receiving chemotherapy, while Muthanna et al reported a lower rate of 41.1%.[19] Ludwig et al found an incidence of 50.4% in patients with solid tumors, and Almehmadi et al reported a 44.1% incidence in Saudi Arabian patients with solid tumors.[20,21]

The present study categorized anemia based on its severity, and the highest number of patients had mild anemia. Iron deficiency anemia was the most common type of anemia in all three categories of anemia, followed by anemia of chronic disease and vitamin B12 deficiency megaloblastic anemia.

In one study, 56.6 percent had mild anemia, 34.2 percent had moderate anemia, and 9.1 percent had severe anemia.[12] Another study found that 29.7 percent of patients with solid tumors had moderate-to-severe anemia.[20] The prevalence of anemia was higher in older patients in some studies. Life-threatening anemia was not seen in any patients in these studies.[8,22]

In our study, anemic patients had predominantly microcytic (55.88%) and macrocytic (8.8%) morphology, which was found to be statistically significant. This is consistent with the findings of Kifle et al, who reported that 47.4 percent of anemia cases were microcytic and 50.5 percent were normocytic.[8] In contrast, Muthanna et al found that the most common types of anemia were normocytic normochromic (75%) and macrocytic polychromic (17.5%).[12]

Iron deficiency anemia and anemia of chronic disease were the most common types of anemia observed in the study population. Females were more likely to experience iron deficiency anemia than males (73.68% versus 26.31%). Megaloblastic anemia was similarly prevalent in both sexes. A study by Muthanna et al reported similar findings with iron deficiency anemia being the most prevalent (75.6%), followed by a lack of vitamin B12 and folic acid (16.7%), and bleeding being the least common cause (7.5%).[12]

In our study of 100 cancer patients, head and neck cancer was the most common, followed by breast, female genital, lung, prostate, gallbladder, and pancreatic cancers. Among anemic patients, the most prevalent types of cancer were gynecological, followed by head and neck, prostate, and lung cancers. However, the correlation between cancer type and anemia was not statistically significant. When we classified malignancies into gynecological and non-gynecological categories, we found a significant association between the presence of anemia and gynecological malignancies, with more incidence in gynecological malignancies. The prevalence of anemia varies depending on the type of cancer.[16,22-24]

According to Kifle et al, gynecologic cancers were the most prevalent, followed by nasopharyngeal, colorectal, soft tissue sarcoma, head and neck cancers.[8] The most frequent form of cancer among the patients reported by Xu et al was breast cancer, followed by lung, colorectal, ovarian, and gastric cancer. Similar findings were reported by Almehmadi et al and Schwartz.[19,21,22] According to Muthanna et al, breast cancer patients had a higher prevalence of anemia, at 41.1 percent, while Ludwig et al found that patients with lung cancer and gynecological malignancies had the highest incidence of anemia.[2,12]

Limitations

The limitations of this study were small sample size and could be selection bias.

CONCLUSION

In conclusion, the study revealed a high prevalence of anemia in newly diagnosed, untreated cancer patients, with iron deficiency anemia being the most common type, followed by anemia of chronic disease. Gynecological malignancies were significantly associated with the presence of anemia. Early diagnosis and monitoring of anemia, especially in patients with gynecological malignancies, can aid in providing appropriate care and maintaining a good quality of life. Regular monitoring of cancer patients, regardless of chemotherapy status, is essential in preventing anemia and reducing morbidity. This should be included in all cancer treatment protocols.

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