

## Original Article



# Prevalence and Classification of Anemia among Patients with Gynecological Malignancies: A Prospective Observational Study from a Tertiary Cancer Institute in North India

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## Abstract

**Background:** Anemia is a frequent comorbidity in women with gynecological malignancies, adversely affecting tolerance to surgery, chemotherapy, and radiotherapy. Despite its clinical relevance, Indian data on its prevalence and severity patterns across tumor sites remain heterogeneous. **Objective:** To estimate the prevalence, severity, and etiological classification of anemia among women with newly diagnosed gynecological cancers presenting for primary management. **Methods:** This prospective descriptive observational pilot study was conducted at a cancer institute in North India, from May 2023 to August 2025. Consecutive women with histologically confirmed carcinoma of the cervix, endometrium, ovary, or vulva who had not received prior treatment for cancer or anemia in the preceding six months were screened. Anemia was defined as hemoglobin < 11 g/dL (NCI 2017 criteria). Eligible participants underwent hematological evaluation including general blood picture, RBC indices, and iron profile for classification and severity grading. **Results:** Of 758 new gynecological cancer patients registered, 282 completed evaluation and treatment. Anemia was detected in 155 patients, giving a prevalence of 55%. Severe anemia (Hb ≤ 7 g/dL) occurred in 18%, moderate in 21%, and mild in 60.6%. Ovarian (44%) and cervical (44%) cancers were the most frequent sites associated with anemia. Advanced stage (FIGO 2B–3C) disease correlated with higher anemia prevalence. Parenteral iron therapy was more frequently administered among ovarian cancer patients, whereas blood transfusions predominated in those undergoing radiotherapy. **Conclusion:** Anemia is a highly prevalent comorbidity in women with gynecological cancers, particularly ovarian and cervical carcinomas, and is more pronounced in advanced disease. Routine pre-treatment screening and proactive correction of anemia are essential to optimize treatment compliance and outcomes.

**Keywords:** *anemia, gynecologic cancer, cervix carcinoma, ovarian cancer, prevalence.*

## Introduction

Anemia is among the most common systemic comorbidities encountered in cancer patients worldwide. In gynecological oncology, it is particularly prevalent because of multifactorial causes including chronic blood loss, nutritional deficiencies, systemic inflammation, and bone marrow suppression. The presence of anemia in cancer patients not only reflects disease burden but also exerts a direct influence on treatment tolerance, efficacy, and overall survival [1,2].

In India, where anemia itself is endemic among women of reproductive age, this problem assumes a much greater magnitude. The National Family Health Survey (NFHS-5) reported anemia prevalence rates of 53% among women aged 15–49 years [5]. The coexistence of underlying nutritional anemia and malignancy-induced anemia presents unique diagnostic and therapeutic challenges, often under-recognized in clinical practice.

In patients with gynecological cancers, anemia can arise from multiple pathophysiological mechanisms. In cervical cancer, chronic vaginal bleeding and nutritional iron deficiency are common contributors [6]. In ovarian malignancies, anemia may be secondary to chronic inflammation, cytokine-mediated erythropoietin suppression, and the anemia of chronic disease pattern [7,8]. Endometrial and vulvar cancers often exhibit anemia related to age-related comorbidities or blood loss rather than tumor infiltration. Moreover, tumor-associated inflammation leads to increased hepcidin expression, blocking intestinal iron absorption and iron release from stores, resulting in functional iron deficiency [8].

The clinical impact of anemia in cancer care is well established. Multiple studies have shown that anemia correlates with reduced tumor oxygenation, which diminishes radiosensitivity and increases resistance to cytotoxic agents [9,10]. This hypoxic microenvironment activates hypoxia-inducible factors (HIFs) that promote angiogenesis, tumor proliferation, and metastatic potential

[9]. Thus, the correction of anemia is not merely supportive care but a critical adjunct to oncologic therapy.

Previous reports from western countries indicate an anemia prevalence ranging from 20% to 30% among gynecologic malignancies [2,3]. However, limited data from India, where delayed presentation, nutritional deprivation, and late-stage disease are more frequent, suggests higher prevalence. A study by Singh et al. (AIIMS, 2021) observed a 58% prevalence of anemia among cervical cancer patients receiving chemoradiation [11], while Tiwari et al. (2022) found rates of 45–50% among ovarian cancer patients [12]. Despite such evidence, most Indian cancer centers lack standardized anemia management protocols or pre-treatment correction algorithms, including that for nutritional supplementation.

Recognizing and addressing anemia in this population is essential for improving treatment tolerance, minimizing transfusion-related risks, and enhancing oncologic outcomes. This prospective study was therefore designed to determine the prevalence, severity, and classification of anemia among patients with newly diagnosed gynecological cancers at a tertiary cancer institute in North India, along with its impact on treatment outcomes.

## Methods

### Study Design and Setting

This was a prospective, descriptive, observational pilot study conducted at the Department of Gynecologic Oncology, in a teaching institute in Uttar Pradesh, India. The study period extended from May 2023 to August 2025. The institute is a tertiary referral cancer center for patients from northern and eastern India, providing multidisciplinary oncologic care. Considering a footfall of 500 patients in 2 years who would attend OPD on any of the 3 days of the week, a sample size of 200 patients was considered for the study. Institutional ethics committee approval was obtained prior to initiation.

### Study Objectives

The primary objective was to determine the prevalence and type of anemia among women newly diagnosed with gynecologic malignancies.

The secondary objectives included:

1. Evaluating the distribution of anemia severity according to the CTCAE v5.0.
2. Determining site-wise patterns of anemia (cervix, ovary, endometrium, vulva).
3. Exploring the association between anemia severity and FIGO stage at presentation.
4. Describing patterns of management strategies (iron therapy vs blood transfusion).

### Eligibility Criteria

#### Inclusion Criteria

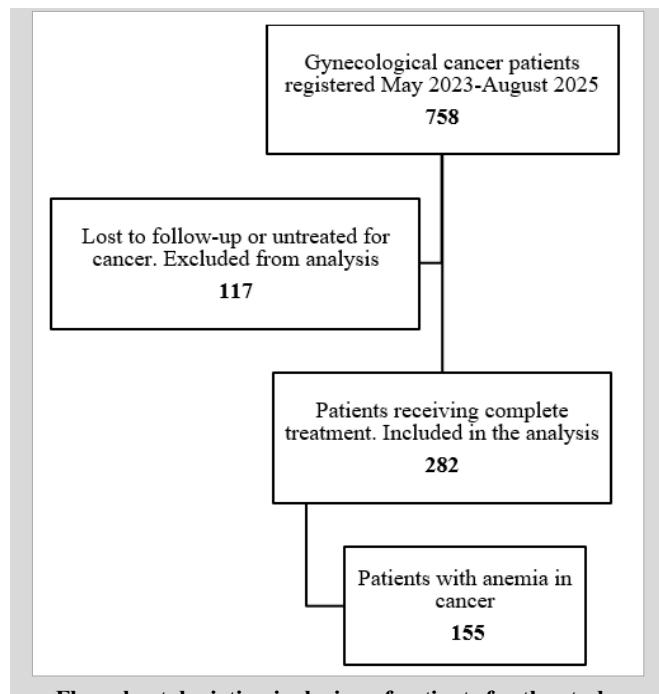
- Women  $\geq 18$  years with histopathologically confirmed carcinoma of cervix, endometrium, ovary, or vulva.
- Newly diagnosed cases within the previous six months.
- No prior cancer-directed treatment (surgery, radiotherapy, chemotherapy, or hormonal therapy).
- No prior anemia-specific therapy (iron, folate, vitamin B12 supplementation, or transfusion) in the preceding six months.
- Hemoglobin  $<11$  g/dL according to NCI (2017) criteria

#### Exclusion Criteria

- Prior cancer therapy within six months.
- Presence of another synchronous malignancy.
- Known hematologic disorder unrelated to cancer.
- Pregnant or lactating women.
- Refusal to undergo treatment or follow-up in the hospital

#### Sampling and Recruitment

Consecutive eligible patients attending the Gynecologic Oncology outpatient clinic on 3 specified days of the week were screened as part of routine OPD based care. Demographic details, cancer site, histopathology, and FIGO staging were recorded. The study flow followed the STROBE framework for observational studies.



Flow chart depicting inclusion of patients for the study.

#### Clinical and Laboratory Evaluation

All enrolled patients underwent baseline hematologic assessment including:

- Hemoglobin (Hb) and hematocrit (Hct) using automated analyzers.
- Red cell indices (MCV, MCH, MCHC, RDW).
- Peripheral smear for morphology.
- Iron studies: serum iron, ferritin, total iron-binding capacity (TIBC), and transferrin saturation were done for those who were treated by iron therapy.

Patients with Hb  $<11$  g/dL and Hct  $<35\%$  were categorized as anemic. Based on CTCAE v5.0, anemia was classified by severity:

- Mild: 10.0–10.9 g/dL
- Moderate: 8.0–9.9 g/dL
- Severe:  $<8.0$  g/dL

Anemia was further classified etiologically into:

- Microcytic hypochromic (iron deficiency pattern)
- Normocytic normochromic (chronic disease pattern)
- Macrocytic (B12/folate deficiency)

## Results

### Study Population

During the study period, 758 newly diagnosed gynecologic cancer patients registered for evaluation, of these, 282 (37%) completed full diagnostic work-up and received treatment at the institute and were thus included in the final analysis.

The mean age of participants was  $50.1 \pm 11.2$  years (range 27–78 years). Majority (72%) were postmenopausal.

**Table 1. Demographic and Clinical Characteristics of Study Participants**

| Parameter               | Mean $\pm$ SD / n (%) | Range |
|-------------------------|-----------------------|-------|
| Age (years)             | $50.1 \pm 11.2$       | 27–78 |
| Postmenopausal women    | 203 (72%)             | —     |
| Total patients analyzed | 282                   | —     |
| Anemic patients         | 155 (55%)             | —     |
| Non-anemic patients     | 127 (45%)             | —     |

**Table 2. Distribution and Severity of Anemia by Cancer Site**

| Cancer Site     | Total Cases (n) | Anemia Present n (%) | Predominant Type        | Severe/Moderate n (%) |
|-----------------|-----------------|----------------------|-------------------------|-----------------------|
| Cervix uteri    | 68              | 30 (44%)             | Microcytic hypochromic  | 18 (26%)              |
| Ovary           | 69              | 30 (44%)             | Normocytic normochromic | 20 (29%)              |
| Endometrium     | 9               | 6 (6%)               | Normocytic              | 2 (22%)               |
| Uterine sarcoma | 4               | 3 (3%)               | Normocytic              | 1 (25%)               |

### Stage-wise Correlation

The FIGO stage at presentation was advanced (Stage IIB–IIIC) in 80% of cervical and 89% of ovarian cancer patients. Severe anemia was significantly more common in advanced-stage disease. Mean hemoglobin demonstrated a progressive decline with advancing FIGO stage, decreasing from 10.05 g/dL in stage I–IIA to 8.70 g/dL

### Prevalence and Severity of Anemia

Among the 282 evaluable patients, 155 (55%) were anemic (Hb  $<11$  g/dL).

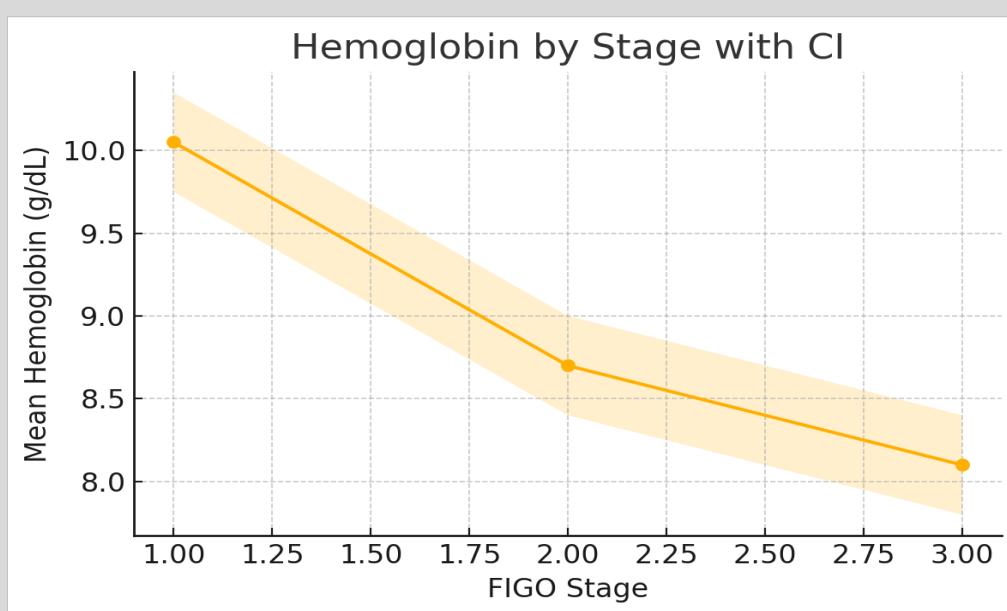
Distribution according to severity was as follows:

- Mild anemia: 94 patients (60.6%) — Mean Hb  $10.5 \pm 0.3$  g/dL
- Moderate anemia: 33 patients (21.2%) — Mean Hb  $8.4 \pm 0.5$  g/dL
- Severe anemia: 28 patients (18.1%) — Mean Hb  $6.7 \pm 0.6$  g/dL

The overall mean hemoglobin across all anemic patients was  $9.2 \pm 1.4$  g/dL.

The distribution of anemia across major cancer sites is summarized in Table 2. Cervical and ovarian cancers together account for 88% of all anemic cases.

in stage IIB–IIIC and 8.10 g/dL in stage IV. Linear regression showed a strong inverse relationship between stage and hemoglobin (regression equation:  $Hb = 10.90 - 0.98 \times \text{stage}$ ). Spearman rank correlation confirmed a perfect monotonic negative association ( $\rho = -1.0$ ,  $p < 0.001$ ). These results indicate that higher disease stage is strongly associated with lower baseline hemoglobin levels.



**Figure 1. Regression Line Equation: Using simple linear regression (FIGO stage coded as 1, 2, 3):**

$$\text{Haemoglobin (g/dL)} = 10.90 - 0.98 \times (\text{FIGO stage})$$

**Slope =  $-0.975$ ; Intercept = 10.900** Interpretation: For every one-stage increase in FIGO stage, mean hemoglobin falls by  $\sim 0.98$  g/dL.

### Morphologic and Etiologic Patterns

Peripheral smear analysis revealed:

- Microcytic hypochromic anemia: 52%
- Normocytic normochromic anemia: 39%
- Macrocytic anemia: 9%

Iron studies showed that iron deficiency (ferritin  $<30$   $\mu$ g/L, low transferrin saturation) accounted for nearly half (48%) of cases, while anemia of chronic disease comprised 41%. Only 7% had combined deficiency, and 4% were attributed to vitamin B12 or folate deficiency based on peripheral blood smear.

## Therapeutic Interventions

Among 155 anemic patients:

- Oral iron therapy and dietary supplementation: 46 (30%)
- Parenteral iron (IV): 57 (37%)
- Blood transfusion: 38 (24%)
- Combined therapy (IV + oral): 14 (9%)

Parenteral iron was more often administered to ovarian cancer patients (n = 34, 60%) preparing for chemotherapy, while blood transfusions were predominantly used for cervical cancer patients receiving concurrent chemoradiation (n = 25, 66%).

## Surgical outcomes of patients with moderate to severe anemia with gynecological cancers

27 patients who had moderate anemia underwent surgical treatment. All patients were of epithelial ovarian cancer. The anemia was corrected by a combination of intravenous iron therapy and blood transfusion. The stage of disease was stage 3C and above with 5 patients with stage 4 disease. All these patients first underwent neoadjuvant chemotherapy followed by interval surgery; stage 4 patients underwent six cycles of chemotherapy before surgery. All patients completed treatment. 1 patient of stage 3c and 3 patients of stage 4 disease developed recurrence within 1 year of treatment, there was no chemoresistance observed in this cohort of patient.

The patients with moderate to severe anemia who had been treated surgically were compared with those who were treated medically. The results show a slightly higher mean hemoglobin level in those treated surgically. (Table 3)

**Table 3: Comparison of patients with moderate to severe anemia treated surgically versus medically**

| Group        | N  | Mean (SD)   | Median (IQR)      |
|--------------|----|-------------|-------------------|
| Surgical     | 23 | 9.37 (1.52) | 9.90 (8.65–10.55) |
| Non-surgical | 47 | 8.99 (1.49) | 9.10 (8.00–10.20) |

## Discussion

The findings of this study corroborate that anemia is highly prevalent (55%) among Indian women presenting with gynecological cancers, affecting more than half of all newly diagnosed patients and this agrees with the study hypothesis of expected prevalence of 50%. Our observed anemia prevalence is like prior Indian studies. Singh et al. reported 58% prevalence among cervical cancer patients undergoing chemoradiation [11,13], while Maurya et al. found 54% among mixed gynecologic malignancies [14]. Conversely, Hufnagel et al. reported only 20% in a U.S. cohort [2]. The prevalence of anemia was higher among ovarian cancer patients when compared to the cervical cancer cohort in our study. Our single-center study is unique in providing a comparison of prevalence of anemia between gynecological cancer subsites. The disparity likely reflects differences in baseline nutritional status, healthcare access, and timing of diagnosis. A 2023 meta-analysis of 27 international studies found a pooled prevalence of 39% among solid tumor patients, confirming higher rates in developing countries [16]. Although several Indian studies have reported similar results, there is no systematic Indian prehabilitation program for managing such patients before active cancer directed treatment, which would include dietary monitoring and physical activity.

## Pathophysiology and Mechanistic Insights

The etiology of anemia in cancer is multifactorial. Iron deficiency, often from chronic tumor-related bleeding (especially in cervical

carcinoma), remains predominant in Indian patients. Anemia of chronic disease arises from inflammatory cytokines-interleukin-6, tumor necrosis factor- $\alpha$ , and interferon- $\gamma$ —which suppress erythropoietin production and impair iron mobilization [7,8,15]. The resulting hepcidin-mediated “iron blockade” explains why oral iron therapy often fails in these patients. Majority patients in this study were treated by parenteral iron therapy or blood transfusion. Oral iron therapy was utilized in mild anemia only.

The anemia adversely affects tumor biology and treatment efficacy. Hypoxia-induced radio resistance is a well-characterized phenomenon in cervical carcinoma, mediated by stabilization of HIF-1 $\alpha$  and subsequent angiogenic signaling [9,10]. Several studies—including those by Thomas *et al.* [12] and Chopra *et al.* [6] have shown that pretreatment hemoglobin <10 g/dL correlates with poor local control, lower disease-free survival, and higher recurrence rates in cervical cancer. Similarly, in ovarian malignancies, low hemoglobin is associated with reduced chemotherapy tolerance and increased treatment interruptions. The ovarian cancer cohort in our study required a greater number of chemotherapy cycles before debulking surgery, while the higher stage had a negative correlation with severity of anemia. Rizzo et al., in their multicenter observational study found that baseline anemia is a negative prognostic factor for epithelial ovarian cancer outcomes [17].

## Management Strategies and Evolving Practices

The management of cancer-associated anemia should be tailored according to etiology and disease setting. Red blood cell transfusion remains the mainstay for rapid correction but should be reserved for symptomatic or severe anemia due to risks of infection, transfusion reactions, and immunomodulation [18].

Parenteral iron therapy is gaining acceptance as an effective and safe alternative. Intravenous iron (ferric carboxymaltose or iron sucrose) replenishes iron stores even in functional iron deficiency states, facilitating erythropoiesis [19,20]. In our study, this approach was favored in ovarian cancer patients receiving chemotherapy, consistent with global best practices.

The role of erythropoiesis-stimulating agents (ESAs) remains debated. Although ESAs effectively reduce transfusion requirements, several studies have raised concerns about increased thromboembolic risk and possible tumor progression [21]. Current NCCN guidelines (2024) recommend their use only in palliative settings or in patients receiving non-curative therapy, targeting Hb  $\leq$ 12 g/dL [22]. Indian consensus guidelines (ICON-G, 2024) similarly advocate individualized use, emphasizing iron repletion before ESA initiation [23]. In our study ESA was given in advanced stage patients receiving treatment with palliative intent.

## Socio-Nutritional and Public Health Dimensions

The backdrop of widespread nutritional anemia in Indian women amplifies the oncologic impact. Most patients already enter cancer care with depleted iron stores and suboptimal nutrition. Integrating routine hemoglobin and ferritin assessment at cancer screening and preoperative clinics could yield significant improvements in treatment readiness [23]. This was observed in our surgical cohort of patients.

## Limitations and Future Directions

The present study is limited by its single-center design, modest sample size, and attrition of untreated patients. Nonetheless, it provides foundational data for multicentric epidemiological mapping of oncologic anemia in India. Future research should focus on:

- Correlating anemia correction with survival,
- Assessing cost-effectiveness of parenteral iron vs transfusion, and
- Evaluating biomarkers like hepcidin, ferritin/transferrin ratios, and reticulocyte hemoglobin content to differentiate iron deficiency from anemia of chronic disease.

### Summary of Key Implications

Our findings reaffirm that anemia is a modifiable prognostic factor in gynecological oncology. Addressing it systematically can improve therapeutic outcomes, reduce fatigue, and enhance overall patient well-being. Implementing standardized institutional algorithms for anemia screening and correction should be a priority.

## Conclusion

Anemia was present in over half of newly diagnosed gynecologic cancer patients, especially in cervical and ovarian malignancies and had a positive correlation with the stage of disease.

## Conflict of Interest

None declared.

## Funding

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## Ethics approval

Approved ID: KSSSCI/IEC/12/72/2023

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