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## **REVIEW ARTICLE**

# HEMATOCRIT AND HEMOGLOBIN RATIO: A POTENTIAL INDICATOR FOR CERVICAL CANCER PROGNOSIS –A NARRATIVE REVIEW

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# Abstract



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**Dr. Emmanuel Ifeanyi Obeagu**, Department of Biomedical and Laboratory Science, Africa University, Zimbabwe. Tel: +234 803 736 9912; E-mail: *emmanuelobeagu@yahoo.com*  Cervical cancer continues to be a major source of cancer-related illness and death among women globally, especially in low- and middle-income nations. Although progress in screening and treatment has enhanced results, discovering straightforward, affordable, and broadly available prognostic indicators is essential, particularly in resource-constrained environments. Hematological measures like hematocrit (Hct) and hemoglobin (Hb) are regularly assessed in clinical settings, and their ratio Hct/Hb has recently been identified as a potentially significant marker for disease progression and treatment response. The Hct/Hb ratio indicates modifications in red blood cell structure, plasma volume, and systemic inflammation elements closely related to tumor biology and anemia associated with cancer. In cervical cancer, alterations in this ratio might relate to tumor hypoxia, inadequate oxygen supply, and inflammatory mechanisms that encourage disease advancement and therapeutic resistance. Initial research has suggested that a diminished or modified Hct/Hb ratio might correlate with later disease stages, lowered treatment effectiveness, and reduced survival rates, indicating its importance as a prognostic factor.

Keywords: Biomarkers, cervical cancer, hemoglobin, hematocrit, tumor microenvironment.

### **INTRODUCTION**

Cervical cancer poses a major public health issue, being the fourth most prevalent cancer in women worldwide. Even with progress in preventive measures like HPV vaccination and enhancements in screening initiatives, the incidence of cervical cancer is still disproportionately elevated in developing nations. Delayed presentation and restricted availability of diagnostic and treatment resources lead to unfavorable results. In these situations, recognizing cost-effective and readily accessible biomarkers for prognosis is essential for enhancing clinical results and directing efficient management<sup>1,2</sup>. Prognostic indicators are essential in cancer treatment since they assist in anticipating disease advancement, treatment effectiveness, and overall survival rates. Classic prognostic factors in cervical cancer encompass tumor stage, lymph node involvement, histological subtype, and treatment options. Nevertheless, these necessitate sophisticated imaging or histopathological evaluation, which may not be easily accessible in every clinical environment. As a result, there is an increasing focus on hematological parameters, which are cost-effective, commonly assessed, and possibly revealing about

disease condition<sup>3,4</sup>. Hematocrit (Hct) and hemoglobin (Hb) are essential elements of the complete blood count (CBC) panel. Hemoglobin is the main molecule that transports oxygen in red blood cells, whereas hematocrit assesses the percentage of blood volume that red blood cells constitute. Both parameters are closely monitored and act as essential indicators of a patient's blood and oxygen levels. Abnormalities outside typical ranges frequently occur in cancers due to reasons like long-term illness, lack of nutrition, or myelosuppression caused by treatment<sup>5,6</sup>.

Recent research has presented the hematocrit-tohemoglobin (Hct/Hb) ratio as a new hematologic marker with possible prognostic significance. In standard physiological circumstances, the Hct/Hb ratio usually falls between 2.9 and 3.3. Deviations from this range may indicate changes in red blood cell shape, microcytosis, macrocytosis, or alterations in plasma volume all of which can happen in cancer patients as a result of systemic inflammation, tumor metabolism, or treatment methods. Consequently, the Hct/Hb ratio could provide a more comprehensive view than Hct or Hb values separately<sup>7</sup>. In cervical cancer, anemia is commonly observed, particularly in individuals with advanced-stage illness. Anemia diminishes quality of life and also leads to tumor hypoxia, linked to a poor response to radiotherapy and heightened tumor aggressiveness. Although hemoglobin levels have historically been seen as indicators of radiotherapy effectiveness, new findings indicate that including Hct values and determining their ratio with Hb could improve prognostic precision. This method indicates the seriousness of anemia as well as the fundamental alterations in red blood cell physiology<sup>8,9</sup>. Additionally, the Hct/Hb ratio might indicate the systemic inflammatory response commonly seen in patients with cervical cancer. Chronic inflammation results in cytokine-driven inhibition of erythropoiesis, functional iron deficiency, and alterations in red blood cell parameters. As cervical cancer advances, these inflammatory processes escalate, possibly changing hematological markers. Consequently, the Hct/Hb ratio may indirectly reflect interactions between the tumor and host, including both metabolic and immune factors that influence the progression of the disease $^{10}$ .

The aim of this narrative review is to explore the role of the hematocrit and hemoglobin ratio (HHR) as a potential prognostic indicator in cervical cancer.

# Cervical cancer and hematologic parameters

As the tumor progresses, it causes systemic impacts that reach well beyond the cervix. Anemia is one of the most commonly seen symptoms in cervical cancer patients and can arise from chronic blood loss due to delicate tumor tissues, nutrient shortages, bone marrow suppression, or the effects of inflammatory cytokines. Anemia, particularly if untreated, can impair tissue oxygen levels and worsen tumor hypoxia a state recognized to enhance radioresistance and deteriorate prognosis. As a result, hemoglobin levels have traditionally served as a proxy indicator for evaluating the appropriateness and anticipated effectiveness of radiotherapy in patients with cervical cancer<sup>11-13</sup>. In addition to hemoglobin, hematocrit a gauge of the percentage of red blood cells in the blood also indicates vital elements of a patient's ability to transport oxygen. Evaluating the hematocrit-to-hemoglobin (Hct/Hb) ratio in conjunction with hemoglobin provides a deeper insight into the structural and volumetric features of red blood cells. Variations in this ratio might indicate microcytosis, macrocytosis, hemoconcentration, or hemodilution conditions linked to fundamental metabolic or inflammatory alterations caused by cancer. Thus, assessing the Hct/Hb ratio may offer further understanding of the pathophysiological mechanisms occurring in individuals with cervical cancer<sup>14-16</sup>

In this context, hematologic parameters serve not only as complementary laboratory values but also as active biomarkers indicating the host's reaction to tumor load. For example, heightened inflammatory indicators like neutrophil-to-lymphocyte ratio (NLR) or platelet-tolymphocyte ratio (PLR) have been associated with negative results in multiple cancers, including cervical cancer. These ratios reflect the systemic inflammatory environment that frequently accompanies tumor advancement and immune evasion. Similarly, alterations in red blood cell measurements reflected by variations in mean corpuscular volume (MCV), red cell distribution width (RDW), and Hct/Hb ratio could indicate disturbances in erythropoiesis and oxygen transport capability<sup>17-19</sup>. The practical use of hematologic parameters stems from their availability, cost-effectiveness, and impartiality. In settings with limited resources, where advanced imaging or molecular diagnostics are inaccessible, these bloodbased markers can act as important supplements for staging, risk assessment, and treatment strategy development. The Hct/Hb ratio shows potential as a prognostic indicator that may notify clinicians of advanced disease, increased tumor hypoxia, or an inadequate systemic environment for treatment<sup>20</sup>.

# The Hematocrit-to-Hemoglobin Ratio (Hct/Hb) in cervical cancer prognosis

The quest for straightforward, dependable, and affordable biomarkers in oncology has led to increased focus on the hematocrit-to-hemoglobin ratio (Hct/Hb) as a possibly important measure of disease condition. Although hematocrit and hemoglobin are commonly evaluated and thoroughly understood elements of the complete blood count, their ratio provides a nuanced, yet insightful perspective for assessing red blood cell morphology and systemic physiology. In cervical cancer, where late-stage detection and treatment resistance are ongoing challenges, the Hct/Hb ratio has become a potential marker that deserves additional clinical investigation<sup>21,22</sup>. Under typical physiological circumstances, the Hct/Hb ratio generally lies within a small range of about 3.0±0.2. Variations from this range could indicate changes in the size, shape of red blood cells, or plasma volume elements affected by disease advancement, nutritional condition, and the body's inflammatory reaction. A lower-than-anticipated Hct/Hb ratio may indicate microcytic anemia typically observed in chronic illnesses or iron deficiency, while a higher ratio could suggest macrocytosis, which might result from deficiencies in vitamin B12 or folate. In cancer patients, these imbalances can be worsened by metabolic disturbances caused by tumors or by bone marrow suppression related to treatment<sup>23,24</sup>. In cervical cancer, the prognostic effects of anemia are well established, with low hemoglobin levels linked to a worse response to radiotherapy, heightened tumor hypoxia, and reduced survival rates. The Hct/Hb ratio enhances this comprehension by considering both the volume and concentration of red blood cells, providing insights into the seriousness of anemia as well as the underlying erythropoietic activity. This differentiation is clinically important, since two individuals with the same hemoglobin levels can exhibit markedly different Hct/Hb ratios, which may indicate varying physiological conditions and risk factors<sup>25,26</sup>. Additionally, the systemic inflammation and metabolic strain caused by cervical cancer can directly influence

strain caused by cervical cancer can directly influence erythropoiesis and red blood cell parameters. Cytokines linked to tumors, including interleukin-6 and tumor necrosis factor-alpha, can suppress erythropoietin production and iron metabolism, resulting in a functional iron-deficiency condition referred to as anemia of chronic disease. These changes affect hematocrit and hemoglobin levels separately and could skew the ratio, offering an overview of the disease's overall effect. In this context, the Hct/Hb ratio could function as an indirect indicator of tumor load and host-tumor interplay<sup>27,28</sup>. Initial research and historical analyses have suggested a link between atypical Hct/Hb ratios and advanced stages of cervical cancer, heightened tumor aggression, and lower overall survival rates. Individuals with markedly changed ratios often exhibit worse clinical profiles, indicating that this straightforward index may assist in early risk assessment and personalized treatment strategies. Nevertheless, the absence of uniform cutoff values and the diversity of study groups pose obstacles to its prompt integration into clinical guidelines<sup>29</sup>. Crucially, the usefulness of the Hct/Hb ratio stems from its widespread accessibility and no extra expense. In contrast to molecular markers or imaging methods that need specialized tools and skills, this ratio comes from standard blood tests that are typically conducted for most patients being evaluated for cancer. Particularly in low-resource environments, where sophisticated diagnostics are scarce, incorporating the Hct/Hb ratio into clinical decisions may improve prognostic evaluations and assist in prioritizing care for patients at high risk<sup>30</sup>.

# Clinical evidence in cervical cancer

Cervical cancer, acknowledged as a preventable but common cancer, still requires focus in the global oncology arena because of its impact in low- and middle-income nations. Clinical proof has been fundamental to progress in its identification, management, and prevention, providing both transparency and intricacy to the unfolding story of disease regulation. The historical application of the Papanicolaou (Pap) smear, alongside the modern incorporation of HPV DNA testing, has continuously influenced the development of cervical cancer screening and early detection methodologies through clinical studies<sup>31,32</sup>. The advancement of clinical understanding concerning cervical cancer has been significantly shaped by epidemiological observations that associate persistent infection with high-risk human papillomavirus (HPV) types especially types 16 and 18 with most invasive cervical cancers. Significant research like the multicentric trials from the International Agency for Research on Cancer established the epidemiological foundation for creating HPV vaccines and transforming international screening guidelines. These studies showed both the causal role of HPV and the protective effects of vaccination, resulting in the adoption of immunization programs that are currently lowering incidence rates in vaccinated groups<sup>33,34</sup>. Clinical trials have offered strong evidence endorsing concurrent chemoradiotherapy as the standard treatment for locally advanced cervical cancer. Research like the crucial Gynecologic Oncology Group (GOG) trials has shown enhanced overall survival and progression-free survival by incorporating cisplatin based chemotherapy alongside radiation therapy. Moreover, recent studies on immune checkpoint inhibitors and targeted treatments are starting to broaden the treatment alternatives for recurrent or metastatic diseases, with drugs such as pembrolizumab demonstrating potential in tumors that are positive for programmed death-ligand 1 (PD-L1) $^{35,36}$ .

Clinical research has also emphasized the significance of personalized treatment tailored to disease progression, histological variations, and factors unique to each patient. For example, early cervical cancer is more frequently treated with fertility-preserving techniques like radical trachelectomy, backed by research indicating similar oncological results compared to more extensive surgeries in appropriately chosen patients. Moreover, the use of minimally invasive surgical techniques has been both supported and questioned by clinical evidence while previous studies highlighted their advantages, the LACC trial's results showing worse outcomes with minimally invasive radical hysterectomy for early-stage cervical cancer have influenced surgical decisions globally<sup>37,38</sup>. Furthermore, observational studies and real-world data have highlighted differences in cervical cancer outcomes, especially in marginalized groups. These studies emphasize the ongoing difficulties of late diagnosis, restricted access to screenings, and unequal availability of treatment. These discoveries have energized public health initiatives to improve community engagement, incorporate point-of-care diagnostic technologies, and reinforce referral systems, particularly in sub-Saharan Africa and certain regions of Asia where the disease burden is notably elevated<sup>39</sup>. Crucially, clinical research has begun to reveal the prognostic value of lab parameters in cervical cancer, such as hemoglobin levels, white blood cell counts, and increasingly, the hematocrit-to-hemoglobin (Hct/Hb) ratio. Though still developing, both retrospective and prospective research is investigating how these standard blood markers could act as substitutes for tumor hypoxia, systemic inflammation, or nutritional status each of which affects treatment response and long-term results. These findings indicate a move cost-effective, employing towards accessible biomarkers in routine clinical practice<sup>40</sup>.

# Mechanistic insights in cervical cancer

Cervical cancer, similar to various other cancers, develops from a complicated sequence of genetic, epigenetic, and environmental changes that convert normal cervical epithelial cells into invasive carcinoma. The mechanistic comprehension of cervical cancer has significantly progressed, propelled by developments in molecular biology, genomics, and cell biology. Central to this process is the ongoing infection from high-risk human papillomavirus (HPV), especially types 16 and 18, which account for most cervical cancer occurrences. Nonetheless, although HPV infection is essential for the onset of cervical cancer, it is insufficient by itself. The change of infected cells into cancerous cells is a complex process that includes a sequence of detailed molecular and cellular occurrences<sup>41,42</sup>. The main process driving the onset of cervical cancer is the incorporation of HPV DNA into the host's genome. This integration interferes with standard cellular functions, particularly those related to cell cycle control. The E6 and E7 oncoproteins of HPV are crucial in this mechanism as they disable two important tumor suppressor proteins p53 and retinoblastoma protein (Rb), respectively. The E6 protein interacts with p53, causing its degradation, thereby hindering the cell's capacity to initiate apoptosis when faced with DNA damage. Conversely, the E7 protein interacts with Rb, releasing E2F transcription factors and promoting cell cycle progression. This disturbance enables unchecked cell growth, a key feature of cancer, and fosters conditions favorable for genomic instability, which speeds up tumor formation<sup>43,44</sup>. In addition to viral oncoproteins, the tumor microenvironment (TME) significantly contributes to the advancement of cervical cancer. The TME consists of diverse cell types such as immune cells, fibroblasts, endothelial cells, and components of the extracellular matrix that interact with tumor cells and affect their behavior. In cervical cancer, the tumor microenvironment is frequently marked by persistent inflammation, which can promote tumor growth and suppress the immune response. Elevated levels of inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- $\alpha$ ) are often found in the blood and tumor tissue of patients, aiding in immune evasion, angiogenesis, and metastasis. Additionally, the existence of immune cells like macrophages, regulatory T cells (Tregs), and myeloidderived suppressor cells (MDSCs) further sustains an immunosuppressive microenvironment, obstructing effective antitumor immunity<sup>45,46</sup>.

At the molecular level, the transition from precancerous lesions (cervical intraepithelial neoplasia, or CIN) to invasive carcinoma is similarly affected by changes in essential signaling pathways. The PI3K/ AKT/mTOR pathway, responsible for controlling cell survival, growth, and metabolism, is often activated in cervical cancer. Activation of this pathway enhances cell survival, movement, and apoptosis resistance, aiding in tumor advancement and metastasis. Likewise, the Wnt/β-catenin signaling pathway, recognized for its function in cell growth and differentiation, is frequently disrupted in cervical cancer. Unusual activation of this pathway aids tumor advancement by increasing the expression of genes related to invasion and metastasis47,48. Recent mechanistic findings have uncovered the important role of epigenetic alterations in the development of cervical cancer. Variations in DNA methylation, histone alterations, and non-coding RNA expression can affect gene expression without changing the fundamental genetic sequence.

Specifically, hypermethylation of tumor suppressor genes and hypomethylation of oncogenes have been associated with cervical cancer development. Furthermore, the involvement of long non-coding RNAs (lncRNAs) and microRNAs in cervical cancer is a significant focus of research, given their ability to influence essential cellular functions like proliferation, migration, and chemotherapy resistance<sup>49,50</sup>. The significance of metabolic reprogramming in cancer has become more evident in recent years. Cancer cells, such as those found in cervical cancer, frequently display modified metabolic pathways to facilitate their swift growth and persistence. The Warburg effect, marked by heightened glucose absorption and lactate

generation even with oxygen available, is frequently seen in cervical cancer cells.

This metabolic change not only meets the energy needs of tumor cells but also creates an acidic microenvironment that enhances invasiveness and resistance to therapy. Grasping the metabolic dependencies of cervical cancer may create new opportunities for treatment, especially in focusing on metabolic enzymes or signaling pathways related to the Warburg effect<sup>51,52</sup>. Crucially, the identification of genetic and epigenetic markers that promote cervical cancer has accelerated the creation of targeted treatments. Investigation into the molecular factors of cervical cancer has resulted in the discovery of possible therapeutic targets including the epidermal growth factor receptor (EGFR), vascular endothelial growth factor (VEGF), and immune checkpoint proteins such as PD-1/PD-L1. Clinical trials are presently assessing the effectiveness of monoclonal antibodies and small molecules aimed at these pathways, yielding some encouraging outcomes. Moreover, immunotherapy, which utilizes the body's immune defenses to combat cancer, has demonstrated promise in treating cervical cancer, especially in individuals with advanced or recurrent cases<sup>53,54</sup>.

# Limitations and considerations in cervical cancer research and management

Even with considerable advancements in the comprehension and treatment of cervical cancer, various limitations and factors persist that present obstacles to both research and clinical results. Despite significant progress in decreasing morbidity and mortality through the implementation of screening programs, HPV vaccination, and innovative treatment methods, challenges remain, especially regarding accessibility, equity, and the intricacies of individual patient responses<sup>55,56</sup>. A major challenge in managing cervical cancer is the worldwide inequality in access to screening and treatment. Although high-income nations have experienced a significant decline in cervical cancer rates due to extensive HPV vaccination and regular cervical screening, numerous low- and middleincome countries continue to bear an excessively large disease burden. Restricted availability of healthcare resources, insufficient awareness, inadequate infrastructure, and cultural obstacles lead to late-stage diagnoses and unfavorable survival rates in these areas. This gap highlights the necessity for customized strategies that cater to the distinct healthcare environments of various nations, stressing the significance of affordable, accessible screening techniques and immunization initiatives<sup>57,58</sup>. A significant limitation in managing cervical cancer is the disease's heterogeneity, seen both at the molecular and clinical levels. Cervical cancer is not a singular illness, as patients frequently exhibit different histologic subtypes, genetic alterations, and diverse reactions to therapy. Although recognizing HPV as a key causal factor is a significant advancement, not all people with HPV infections develop cancer. Moreover, additional elements like immune reactions, genetic vulnerability, and environmental factors might affect disease progression, making it more challenging to identify

populations at risk. This variability can complicate the establishment of universally effective treatment protocols, emphasizing the necessity for tailored strategies grounded in molecular characterization and specific patient profiles<sup>59,60</sup>.

The constraints of existing screening technologies continue to be a worry. Conventional screening techniques like the Pap smear, although very effective, can be prone to human mistakes and might miss early lesions in specific groups, particularly in settings with limited resources. Moreover, although HPV DNA testing has enhanced detection rates, it continues to encounter issues concerning affordability, availability, and the emotional stress linked to false-positive outcomes, which may result in needless follow-up tests and higher healthcare expenses. Although liquid-based cytology and HPV testing have become popular, they are not universally accessible or affordable, highlighting the need for the creation of more economical, point-of-care diagnostic tools for wider application<sup>61,62</sup>. Therapeutic approaches, especially for advanced cervical cancer, also encounter restrictions. Despite concurrent chemoradiotherapy being the primary treatment for locally advanced disease, high recurrence rates persist, and the outlook for metastatic or recurrent cervical cancer continues to be unfavorable. Furthermore, the adverse effects of intensive therapies can greatly impact patients' quality of life, leading to enduring complications like infertility, sexual dysfunction, and problems with bowel and bladder functions. The pursuit of more specific therapies and individualized treatment plans influenced by the tumor's molecular profile continues, yet many of these strategies are still in the experimental phase, and their clinical use is still restricted<sup>63,64</sup>.

Immunotherapy has become a hopeful treatment alternative for cervical cancer, particularly in recurrent and metastatic situations. Yet, difficulties persist in determining which patients will benefit from immune checkpoint inhibitors like pembrolizumab and nivolumab. The intricacy of the tumor microenvironment, coupled with the immune evasion tactics used by cervical cancer cells, signifies that not every patient will gain from these treatments. Furthermore, the elevated expenses and the requirement for biomarker testing prior to starting treatment restrict the broad adoption of immunotherapy in resource-limited environments<sup>65-67</sup>. Although progress in genetic and epigenetic studies is revealing new biomarkers and possible therapeutic targets, implementing these discoveries in clinical settings brings its own challenges. The molecular diversity of cervical cancer, along with the shortcomings of existing diagnostic and prognostic indicators, complicates the creation of dependable biomarkers for guiding treatment choices. Moreover, although an increasing amount of evidence endorses the utilization of blood-based markers like the hematocrit-to-hemoglobin (Hct/Hb) ratio, further comprehensive and methodologically sound clinical trials are needed to confirm these results and define their significance in standard clinical procedures<sup>68,69</sup>.

# Practical clinical guidelines for implementing Hematocrit-to-Hemoglobin Ratio (hhr) monitoring in cervical cancer

- 1. Integrating HHR as a routine prognostic tool
  - Monitoring HHR in cervical cancer patients: Clinicians should consider routinely monitoring the hematocrit-to-hemoglobin ratio (HHR) as part of the comprehensive assessment of cervical cancer patients, particularly for those with advanced stages of the disease. Since alterations in HHR may reflect tumor burden, anemia, or systemic inflammation, its inclusion could offer valuable insights into disease progression, treatment response, and overall prognosis.
  - Frequency of monitoring: In patients undergoing active treatment (e.g., chemotherapy or radiation), HHR should be monitored at regular intervals, especially before and after each cycle, to evaluate the effects of therapy on the hematologic profile. In advanced-stage or recurrent disease, more frequent monitoring may be necessary to track disease progression and identify potential complications early.
  - HHR in staging and risk stratification: HHR may provide complementary information to traditional staging systems such as FIGO (International Federation of Gynecology and Obstetrics) for cervical cancer. Elevated HHR may indicate poor prognosis, and as part of a broader clinical evaluation, it can help categorize patients into higher-risk groups who may require more intensive monitoring and treatment. This could aid in clinical decision-making for selecting appropriate interventions.

2. Addressing anemia and its implications in treatment

- Anemia Management: Cervical cancer patients, particularly those with advanced stages, often present with anemia as a result of the disease itself or as a side effect of treatment. Clinicians should regularly assess for anemia using both HHR and traditional parameters such as hemoglobin levels and red blood cell counts. Identifying anemia early in the treatment process allows for timely interventions (e.g., iron supplementation, erythropoiesis-stimulating agents, or blood transfusions) to improve patient outcomes, optimize treatment tolerance, and enhance quality of life.
- Linking HHR with hematologic support: A declining HHR may be indicative of worsening anemia or deterioration in red blood cell production, which may warrant hematologic support measures. Clinicians should be aware of the potential need for blood transfusions in patients with significantly low hemoglobin and hematocrit levels, ensuring that these measures are implemented as needed based on HHR values.

# 3. Personalized monitoring and risk prediction

• Tailoring HHR use to individual patient profiles: The utility of HHR monitoring in cervical cancer prognosis may vary depending on

individual patient characteristics, such as age, comorbidities, and the type of treatment regimen being followed. For example, patients with preexisting cardiovascular conditions may benefit more from frequent HHR monitoring to prevent complications related to anemia or circulatory issues. Additionally, patients receiving aggressive chemotherapy or radiation may need more intense monitoring to detect early signs of bone marrow suppression.

• Incorporating HHR into multimodal prognostic models: Clinicians should integrate HHR monitoring with other clinical, imaging, and molecular data to form a more comprehensive prognostic model. HHR should not be used in isolation but as part of a broader evaluation that includes tumor markers, imaging findings, and patient symptoms. This holistic approach will enable clinicians to better assess the patient's risk profile and guide individualized treatment strategies.

### 4. Evaluating HHR in post-treatment follow-up

- Long-term surveillance: After the completion of primary treatment (e.g., surgery, chemotherapy, or radiation), regular HHR monitoring should be part of the long-term follow-up protocol to detect signs of recurrence or metastasis. A rising HHR could be a red flag, signaling potential tumor progression or emerging complications such as anemia or organ dysfunction.
- HHR as a marker for response to treatment: In patients undergoing neoadjuvant therapy or treatment for recurrent disease, HHR may provide early clues about treatment efficacy. If HHR is significantly elevated or does not improve in response to therapy, clinicians should consider adjusting treatment plans and re-evaluating the patient for potential resistance or suboptimal response to the current regimen.

#### 5. Collaboration and interdisciplinary care

- Multidisciplinary team involvement: Monitoring HHR should be a part of a multidisciplinary care plan, where oncologists, hematologists, and other specialists collaborate to ensure optimal care. In cases where HHR abnormalities are detected, early consultation with hematology or transfusion medicine specialists may be beneficial for refining management strategies and avoiding unnecessary delays in treatment.
- Educational support for patients and caregivers: Clinicians should educate patients and their caregivers about the significance of hematologic monitoring, including the implications of abnormal HHR. Patients should be informed that regular blood tests and HHR monitoring are essential to track treatment progress and identify any complications early. Providing this information helps engage patients in their care and can improve adherence to monitoring schedules.

#### CONCLUSIONS

Cervical cancer continues to be a significant global health issue, with notable differences in incidence, treatment, and results among various populations. Comprehending the fundamental processes of cervical cancer, especially the functions of HPV infection, immune evasion, and the tumor microenvironment, has provided important insights into the causes and advancement of the disease. Despite progress in screening techniques, vaccination initiatives, and therapeutic treatments reducing the impact of cervical cancer, there are still challenges in early detection, treatment, and patient categorization. The ratio of hematocrit to hemoglobin (Hct/Hb) has become a notable potential biomarker for predicting outcomes in cervical cancer. Research indicates that this basic blood parameter might be an effective marker for disease severity, tumor advancement, and patient prognosis. Nevertheless, although its promise as a predictive instrument is intriguing, additional studies are required to confirm its effectiveness in various patient groups and clinical environments. The Hct/Hb ratio, included in a wider array of biomarkers, may enhance current diagnostic and prognostic methods, ultimately advancing personalized treatment approaches and patient management.

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# **AUTHOR'S CONTRIBUTION**

**Obeagu EI:** conceived the idea, writing the manuscript, literature survey. **Goryacheva OG:** formal analysis, critical review. Final manuscript was checked and approved by the both authors.

#### DATA AVAILABILITY

Data will be made available on request.

#### **CONFLICT OF INTEREST**

There are no conflicts of interest in regard to this project.

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