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REVIEW ARTICLE

MENTZER INDEX IN EARLY BREAST CANCER: A LOW-COST DIAGNOSTIC INSIGHT INTO ANEMIA PATTERNS

Emmanuel Ifeanyi Obeagu[1]*, Salma Abdi Mahmoud[2]
[1]*Department of Biomedical and Laboratory Science, Africa University, Muatre, Zimbabwe.*
[2]*Department of Obstetrics and Gynaecology, School of Health and Medical Sciences, The State University of Zanzibar, Zanzibar Tanzania.*

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***Address for Correspondence:**
Dr. Emmanuel Ifeanyi Obeagu, Department of Biomedical and Laboratory Science, Africa University, Zimbabwe. Tel: +263-778025658
E-mail: *emmanuelobeagu@yahoo.com*

Abstract

Anemia continues to be one of the most common and overlooked complications in early breast cancer, caused by inflammation related to tumors, iron storage, and treatment-induced suppression of the bone marrow. Determining the root cause of anemia is essential for enhancing treatment and improving patient results. This review examines the potential diagnostic significance of the Mentzer index a ratio of mean corpuscular volume to red blood cell count as a straightforward, affordable method for distinguishing anemia patterns in early breast cancer. Historically utilized to differentiate iron deficiency anemia from thalassemia trait, recent findings indicate that MI might also represent the erythropoietic and inflammatory changes linked to malignancy. A narrative review method was utilized, consolidating existing literature (2015–2024) regarding the mechanisms of anemia in breast cancer, red blood cell indices, and biomarkers for iron metabolism. Research from PubMed, Scopus, and Google Scholar was evaluated to investigate the diagnostic and pathophysiological connections between the Mentzer index and anemia associated with cancer. Results show that increased MI values in early breast cancer frequently relate to functional iron deficiency due to hepcidin-induced iron blockage and inflammation-related suppression of erythropoiesis. On the other hand, low or normal MI levels might indicate mixed or nutritional anemia conditions. Incorporating MI with biomarkers like ferritin, transferrin saturation, and red cell distribution width improves diagnostic accuracy, especially in resource-constrained environments. The Mentzer index, while rooted in tradition, could offer a significant hematologic insight into anemia types in early breast cancer, enabling personalized interventions and enhanced treatment preparedness.
Keywords: Anemia, breast cancer, early detection, hematological markers, Mentzer index.

INTRODUCTION

Anemia is a common and clinically important comorbidity in women with breast cancer, impacting life quality, treatment tolerance, and overall outlook. In early breast cancer, anemia frequently appears as an initial systemic sign of the tumor's metabolic and inflammatory effects on blood cell production. The root factors are diverse spanning from iron storage and cytokine-induced suppression of erythropoiesis to nutritional shortages, hidden bleeding, or early infiltration of the marrow. Prompt recognition of the anemia subtype is crucial to direct suitable management, avert unnecessary supplementation, and enhance treatment preparedness prior to chemotherapy or radiotherapy[1-3]. Historically, the Mentzer index (MI) derived from the ratio of mean corpuscular volume (MCV) to red blood cell (RBC) count has acted as an uncomplicated hematologic method to distinguish iron deficiency anemia (IDA) from thalassemia trait. An MI above 13 usually indicates iron deficiency, whereas a value below 13 suggests thalassemia. Nevertheless, new findings regarding cancer-related anemia have broadened the significance of traditional red cell indices, as inflammation linked to tumors and functional iron deficiency create morphological characteristics that resemble microcytic anemia. These changes can affect MCV and RBC measurements, indirectly shown in the Mentzer index[4-6].

Recent progress in tumor biology has shown that breast cancer cells actively alter systemic iron balance to support rapid growth and oxidative metabolism. The increased production of hepcidin, a peptide that regulates iron, restricts the availability of iron to

erythroid precursors and sequesters iron within macrophages, leading to functional iron deficiency even when stores are sufficient. At the same time, inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) inhibit erythropoiesis, leading to anemia of chronic disease (ACD). These mechanisms frequently lead to slight hematologic variations that can be identified in standard complete blood count (CBC) metrics well in advance of evident anemia emerging[7-10]. In this scenario, the Mentzer index could provide a straightforward, affordable, and insightful diagnostic glimpse into the initial hematologic changes associated with breast cancer. Its ease of use and dependence on standard CBC data render it especially useful in low-resource environments, where extensive iron studies or hepcidin tests might not be easily accessible. While the MI cannot substitute for molecular or biochemical markers, utilizing it as an auxiliary screening tool can assist clinicians in differentiating between anemia caused by iron deficiency and that driven by inflammation, thus informing personalized patient management[11-14].

Additionally, analyzing anemia patterns through indices like MI could offer indirect perspectives on tumor hypoxia, metabolic changes, and systemic inflammation, which are recognized to affect breast cancer advancement and treatment efficacy. The revived focus on hematologic indices indicates a wider movement towards using regular lab data for personalized oncology an approach that integrates cost-effectiveness with clinical significance[15-18]. Thus, this review intends to critically analyze the diagnostic and pathophysiological significance of the Mentzer index in early breast cancer-associated anemia, emphasizing its potential as a useful complement to contemporary hematologic assessment. This narrative review reevaluates a traditional hematologic marker in a modern oncological context by combining up-to-date evidence on iron metabolism, inflammation, and erythropoietic dynamics, highlighting its significance in clinical settings as well as in resource-constrained situations.

The aim of this review is to evaluate the role of the Mentzer index in the identification and differentiation of anemia in breast cancer patients, particularly in the early stages of the disease and during chemotherapy treatment.

Anemia is a common yet frequently underestimated issue in early breast cancer, arising from intricate interactions between tumor-induced inflammation, iron imbalance, and bone marrow suppression. Timely identification of the anemia subtype is crucial for ensuring proper management, avoiding treatment delays, and enhancing therapeutic results[19-21]. Although the Mentzer index (MCV/RBC ratio) was initially created to distinguish iron deficiency anemia from thalassemia trait, increasing evidence shows that comparable microcytic and hypochromic patterns can occur in cancer-related anemia due to functional iron deficiency and cytokine-induced suppression of erythropoiesis. This presents a chance to view the index as an affordable, easy-to-use screening tool that can offer insights into the hematologic and inflammatory conditions of breast cancer patients especially useful in low-resource environments where extensive iron studies are scarce[22-25]. Therefore, this review intends to assess the possible usefulness of the Mentzer index as a supplementary diagnostic tool in early anemia related to breast cancer, examining its pathophysiological foundation, interpretative significance, and consequences for clinical choices and upcoming research.

METHODS

This study adopted a narrative review approach to synthesize current evidence on the diagnostic and clinical significance of the MI in anemia associated with early breast cancer. Literature was retrieved from PubMed, Scopus, Web of Science, and Google Scholar using combinations of key terms such as “Mentzer index”, “anemia”, “breast cancer” “iron metabolism” “erythropoiesis” and “inflammation”. Articles published between 2015 and 2024 were considered, with earlier seminal works included for conceptual context. Eligible sources included original research articles, clinical studies, systematic reviews, and relevant hematology–oncology reports focusing on anemia mechanisms, red cell indices, or iron dysregulation in breast cancer. The search prioritized studies involving adult female breast cancer patients, excluding pediatric, hematologic malignancy, and unrelated anemia studies. Key information was qualitatively synthesized to highlight the mechanistic basis, diagnostic interpretation, and clinical implications of the Mentzer index in early breast cancer.

Pathophysiology of anemia in breast cancer

Anemia in breast cancer results from a complex interaction of inflammation, iron imbalance, nutritional shortages, and treatment-associated elements. Persistent inflammation in the tumor microenvironment stimulates the secretion of cytokines like IL-6, TNF-α, and IFN-γ, leading to increased hepcidin levels and the inhibition of iron export via ferroportin blockade. This process leads to functional iron deficiency, where iron reserves are sufficient but inaccessible for hemoglobin production[26-29]. Breast cancer cells worsen this imbalance by sequestering iron for their growth requirements a process known as tumor iron addiction. Malignant cells divert iron from normal erythropoiesis by upregulating transferrin receptors and downregulating iron storage proteins, resulting in microcytosis and lower red cell indices[30-34].

Furthermore, deficiencies in nutrients such as iron, folate, and vitamin B12 can hinder red blood cell production, while inflammation or prior treatment exposure leading to marrow suppression results in additional hematologic deterioration. Even though tumor hypoxia promotes erythropoietin (EPO) production, ongoing inflammation frequently leads to EPO resistance, exacerbating anemia[35-39]. These interconnected mechanisms demonstrate both systemic and tumor-induced disruptions in iron metabolism, rendering anemia a clinically significant yet often

overlooked aspect of early breast cancer. In this context, the Mentzer index (MCV/RBC count) can act as a straightforward and useful indicator to distinguish iron deficiency anemia from inflammation-induced microcytosis, offering an economical diagnostic perspective on the metabolic and hematologic changes that arise in early disease[40-45].

Role of Mentzer index in early detection of anemia in breast cancer

The MI, determined by the ratio of MCV to RBC count, is commonly utilized to distinguish iron deficiency anemia from thalassemia trait. In the realm of early breast cancer, its use goes beyond traditional hematology, providing an easy, accessible means to detect developing anemia trends linked to metabolic and inflammatory alterations caused by the tumor[46-48]. Increased MI values could indicate functional iron deficiency caused by hepcidin-induced iron retention and inflammatory inhibition of erythropoiesis, whereas low or borderline values may suggest mixed anemia types or microcytosis similar to thalassemia-like patterns. Incorporating MI with standard laboratory results enables clinicians to obtain early insights into anemia subtypes, which is essential for directing suitable interventions, enhancing treatment readiness, and preventing indiscriminate iron supplementation that could be ineffective or even harmful in cases of inflammation-related anemia[49-51].

Additionally, in settings with limited resources, the Mentzer index serves as an affordable alternative marker for initial hematologic assessment, providing early direction when advanced iron tests or cytokine evaluations are not accessible. Although MI by itself cannot conclusively determine the cause of anemia, adding it to standard blood count evaluations may promote prompt identification of hematologic issues, enhance tailored patient management, and reveal early systemic impacts of breast cancer on erythropoiesis[52,53].

The diagnostic value of Mentzer index in breast cancer patients

The MI provides a hands-on method for assessing anemia in early-stage breast cancer, indicating minor alterations in red blood cell structure resulting from inflammation caused by the tumor and issues with iron regulation. Originally created to differentiate iron deficiency anemia from thalassemia trait, MI can offer indirect understanding of the mechanisms behind cancer-related anemia, especially when more sophisticated diagnostic tests are not accessible[54-57]. In patients with breast cancer, high MI levels frequently reflect functional iron deficiency due to hepcidin-driven iron sequestration, while low or borderline MI levels could suggest mixed anemia types or anemia resulting from chronic inflammation. Through the examination of the MI in conjunction with routine laboratory indicators like hemoglobin, RDW, ferritin, and transferrin saturation, healthcare providers can perform an initial classification of anemia types and direct suitable treatments[58-62].

The diagnostic significance of MI is especially evident in low-resource environments, acting as an affordable, readily accessible proxy indicator to identify patients who might need additional hematologic assessment or specific iron treatment. Although MI is not a conclusive diagnostic method, integrating it into standard complete blood count evaluations improves the early identification of anemia, aids in tailored patient management, and might offer insights into metabolic and inflammatory processes linked to tumors that affect disease progression and treatment outcomes[63-67].

Advantages and limitations of the Mentzer index

The Mentzer index, derived from the ratio of mean corpuscular volume (MCV) to red blood cell count (RBC), is commonly utilized in clinical settings to distinguish various forms of anemia, especially in individuals with microcytic anemia. Its straightforwardness, affordability, and user-friendliness render it an essential resource for initial anemia screening and management[69]. Yet, similar to any diagnostic examination, it presents both benefits and drawbacks that need to be considered in its medical use. Grasping these can assist clinicians in making well-informed choices about using it for diagnosing and treating anemia, especially in complicated situations such as breast cancer[70].

Advantages of the Mentzer index

1. Simplicity and Cost-Effectiveness: One of the key advantages of the Mentzer index is its simplicity. The index relies on two commonly measured parameters in routine blood tests MCV and RBC making it an easily accessible diagnostic tool[69]. Since these parameters are typically included in a standard complete blood count (CBC), there is no need for additional or expensive testing. This cost-effectiveness makes the Mentzer index particularly useful in resource-limited settings where advanced diagnostic tests may not be available[71].

2. Quick and easy calculation: The Mentzer index provides rapid results and can be calculated in seconds. This makes it an excellent tool for clinicians who need to make quick decisions about the management of anemia[72]. The index's quick turnaround time enables healthcare providers to promptly assess the cause of anemia, whether it is due to iron deficiency or a hemoglobinopathy like thalassemia, and decide on the appropriate course of treatment[51].

3. Differentiation between iron deficiency anemia and thalassemia: The Mentzer index is particularly useful in distinguishing between two common types of microcytic anemia IDA and thalassemia[22]. Iron deficiency anemia generally presents with a Mentzer index greater than 13, suggesting that it is related to iron deficiency, whereas values lower than 13 are more likely to be indicative of thalassemia or other hemoglobinopathies[68]. This differentiation is critical because the treatment for these conditions is quite different, with iron supplements used for IDA and blood transfusions or iron chelation for thalassemia.

4. Use in routine screening: Since the calculation of the Mentzer index only requires data from a routine CBC, it is an ideal tool for initial screening of anemia in various patient populations, including those with cancer, such as breast cancer patients undergoing chemotherapy[46]. In these patients, anemia is common, and early identification of the cause can lead to better

management, minimizing treatment delays and improving patient quality of life.

5. Potential for early intervention: By identifying the type of anemia early, the Mentzer index facilitates timely therapeutic interventions. For instance, recognizing iron deficiency anemia can lead to early iron supplementation or dietary adjustments, reducing the impact of anemia on a patient's energy levels and treatment tolerance[73]. This proactive approach can prevent complications, such as severe fatigue or an impaired ability to continue cancer treatment, which is critical for patients with breast cancer undergoing chemotherapy[46].

Limitations of the Mentzer index

1. Not useful for all types of anemia: The primary limitation of the Mentzer index is that it is designed to differentiate between microcytic anemias, specifically iron deficiency anemia and thalassemia. It does not provide insight into other forms of anemia, such as anemia of chronic disease (ACD) or macrocytic anemia caused by vitamin B12 or folate deficiencies. Anemia of chronic disease, commonly seen in cancer patients, often presents with normal or slightly reduced MCV values and cannot be accurately identified using the Mentzer index alone. Additional tests are required to diagnose these types of anemia.

2. Limited in complex cases: In cases of anemia caused by multiple factors or in the presence of comorbidities, the Mentzer index may not provide a clear diagnosis. For example, patients with both iron deficiency and a hemoglobinopathy, such as thalassemia trait, may have a misleading Mentzer index that does not correctly differentiate between the two causes. In such situations, further investigation, including serum ferritin levels, hemoglobin electrophoresis, or genetic testing, is needed to confirm the underlying etiology.

3. Not effective in severe cases of thalassemia: In patients with severe forms of thalassemia, the Mentzer index may not be as reliable. These patients may have large fluctuations in their MCV and RBC count due to the severity of their condition, leading to an inaccurate calculation of the index. Thus, while the Mentzer index is generally useful for identifying milder cases of thalassemia, it is not always accurate in more severe instances, where a more detailed diagnostic approach is required.

4. Potential for misinterpretation in certain populations: The Mentzer index is based on population averages of MCV and RBC, which means it may not account for individual variations, particularly in patients with unusual hematological profiles. For example, patients with conditions such as sickle cell disease, anemia due to kidney disease, or other rare hematological disorders may present with atypical MCV or RBC values that make the Mentzer index less reliable. Additionally, ethnic differences in RBC morphology and size may influence the utility of the index in certain populations, leading to potential misdiagnosis.

5. Not a standalone diagnostic tool: While the Mentzer index can provide valuable information, it should not be used as a standalone diagnostic tool. It should be considered alongside other clinical assessments, patient history, and laboratory tests. Iron studies, hemoglobin electrophoresis, and genetic testing are often necessary to fully understand the cause of anemia, particularly in breast cancer patients who may be receiving chemotherapy or have other underlying conditions that complicate the anemia diagnosis.

Clinical implications and future directions

The use of MI in early breast cancer goes beyond its conventional function of distinguishing iron deficiency anemia from thalassemia[70,71]. In the context of oncology, MI acts as an inexpensive, easily accessible metric that indicates the inherent balance among iron availability, inflammation, and erythropoietic function[72,73]. Increased MI values can suggest functional iron deficiency caused by tumor-related hepcidin production, whereas normal or borderline values may indicate mixed or nutritional anemia types[74,75].

Identifying these differences is clinically significant. Correct understanding of MI can lead to targeted anemia management, avoid unnecessary iron supplementation in inflammatory anemia, and enhance treatment preparation before chemotherapy or radiotherapy. In settings with limited resources where comprehensive iron studies are not commonly available, MI provides an easy substitute marker to aid in diagnostic and treatment choices[76,78]. In the future, research should focus on confirming MI thresholds particular to cancer-related anemia, evaluating its predictive significance for treatment response and fatigue, and examining its combination with other blood indices like RDW, NLR, and ferritin levels to enhance diagnostic accuracy. To establish if MI dynamics can act as an early sign of metabolic or inflammatory changes induced by tumors, longitudinal and multicenter research is necessary[79-81].

CONCLUSIONS

Anemia in early breast cancer is a complex condition resulting from inflammation caused by tumors, disrupted iron metabolism, and hindered red blood cell production, significantly affecting patient quality of life, treatment tolerance, and overall outlook. The MI, typically used to differentiate iron deficiency anemia from thalassemia, provides an inexpensive, accessible insight into these blood-related changes. When assessed together with standard laboratory metrics, MI can assist in the early detection of anemia types, shape customized management approaches, and support clinical decisions, especially in resource-constrained environments. Even though the MI is not a conclusive diagnostic instrument, incorporating it into routine hematologic evaluation offers clinicians a useful supplement for initial anemia assessment. Future research should aim to validate MI thresholds particular to cancer-related anemia, examine its prognostic significance, and evaluate its effectiveness in directing personalized interventions. This review highlights the potential of straightforward, standard laboratory assessments to improve early detection,

refine patient care, and promote fair management of anemia in breast cancer by reassessing a traditional hematologic index through a modern oncology perspective.

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AUTHOR'S CONTRIBUTION

Obeagu EI: conceived the idea, writing the manuscript, literature survey. **Mahmoud SA:** formal analysis, data processing. Final manuscript was checked and approved by both authors.

DATA AVAILABILITY

The empirical data used to support the study's conclusions are available upon request from the corresponding author.

CONFLICTS OF INTEREST

The authors declare no conflict of interest

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None to declare.

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