RESEARCH PAPER

PERIPHERAL SMEAR FINDING IN PANCYTOPENIA

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ABSTRACT

Introduction

Pancytopenia refers to a condition in which there is a decrease in the number of red blood cells, white blood cells, and platelets. Peripheral smear examination is another critical first-line testing that can be used to identify underlying diseases.

Aim

This study compared the diagnostic relevance of peripheral smear results in pancytopenia.

Materials and Methods

A literature review based on the secondary qualitative investigation was conducted using recent studies in hematology and medical databases published between 2021 and 2026.

Results

Findings were common and included macro-ovalocytes, blast cells, dysplastic neutrophils, anisopoikilocytosis, and thrombocytopenia. Early screening, discrimination of diseases, and bone marrow examination advice were facilitated by a peripheral smear.

Conclusion

Peripheral smear is an affordable and available diagnostic test that enhances the early diagnosis of cases of pancytopenia when it is coupled with clinical and bone marrow results.

Keywords: Pancytopenia, Peripheral smear, Hematological disorders, Bone marrow, Cytopenia, Morphology.

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Introduction

Background of the Study

Pancytopenia is a blood disorder which is characterized by the simultaneous decrease in red blood cells (RBCs), white blood cells (WBCs), and platelets in the peripheral blood. It is not a disease but a clinical effect of a number of underlying conditions, such as megaloblastic anemia, aplastic anemia, leukemia, infections, and bone marrow failure syndromes. According to recent studies, the causes of pancytopenia have continued to be among megaloblastic anemia and aplastic anemia in developing countries (Çordan et al.,2025). Clinical significance of the condition is due to the possibility of patients exhibiting severe anemia, frequent recurring infections, and bleeding. Nevertheless, the diagnosis of pancytopenia is also difficult as it has various etiologies and similar clinical appearances. Peripheral smear examination offers quick morphological clues and aids in early screening of severe hematological diseases despite the subsequent invasive examinations (Chew and Kamangar, 2024).

Problem Statement

There are several causes of pancytopenia, including nutritional deficiencies and malignant bone marrow conditions, amongst others, and pancytopenia is not easily diagnosed. The timely clinical diagnosis could have a morbidity and mortality impact, particularly in cases of leukemia and aplastic anemia. Even though bone marrow biopsy is reputed to be definitive, it is also invasive, costly, and not always readily available. Thus, the peripheral smear test is a highly important type of primary, inexpensive diagnostic test that can give initial evidence on the additional morphological samples and direct other hematological studies (Chew and Kamangar, 2024).

Research Aim

The aim was to assess the diagnostic value of peripheral smear results in pancytopenia and how the results can be used to diagnose underlying hematological conditions.

Research Objectives

- To discover typical peripheral smear observations in pancytopenia.
- To relate the morphology of the smears to specific diseases.
- To determine the diagnostic value of peripheral smear examination.
- To compare its contribution towards early diagnosis.

Research Questions

1. What are the typical peripheral smear findings in pancytopenia?
2. What do smear results aid in diagnosing diseases?
3. What is the diagnosis of peripheral smear examination?
4. What is the effectiveness of smear analysis on early detection?

Literature Review

Introduction

Hematological analysis is valuable in determining the underlying pathophysiology of pancytopenia and informing the provision of early clinical care. Peripheral smear examination, which is a type of laboratory examination, is a cheap, fast, and simple diagnostic method among other laboratory investigations. Recent research pointed out that the analysis of peripheral smears may offer significant morphological clues in approximately 70-80 % of hematological diseases prior to any invasive bone marrow examinations being conducted (Lewis and Pozdnyakova, 2023).

Concepts & Hematological Basis

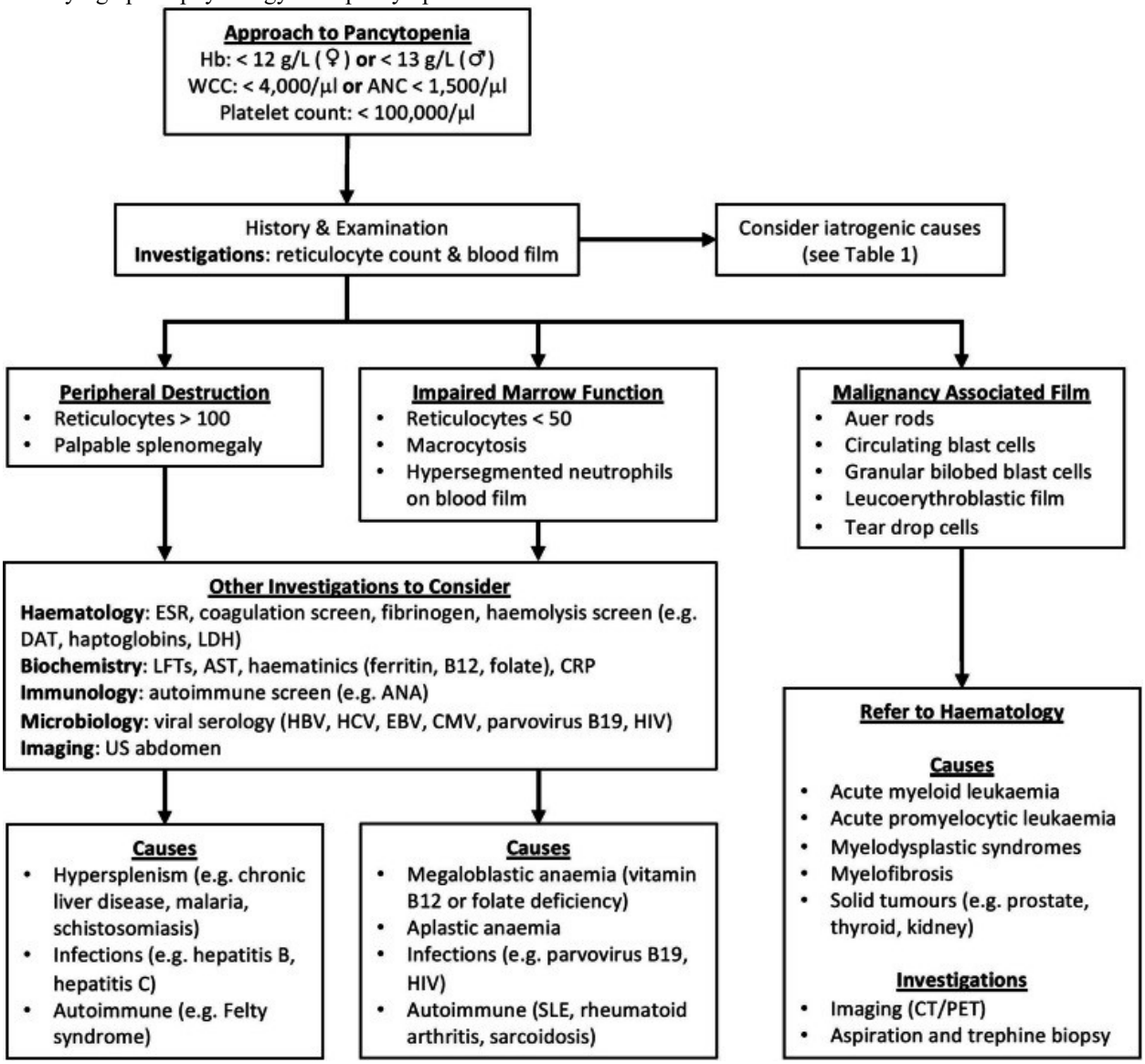

Figure 1: Algorithm for approaching pancytopenia
(Source: Chew, and Kamangar, 2024)

Pathophysiology of Pancytopenia

Cause	Mechanism
Megaloblastic anemia	Ineffective hematopoiesis
Leukemia	Marrow infiltration
Aplastic anemia	Bone marrow failure
MDS	Dysplastic hematopoiesis

Table 1: Causes of Pancytopenia

(Source: Self-created)

Pathophysiology of pancytopenia primarily includes decreased blood cell production, enhanced peripheral blood cell destruction, or inappropriate blood cell sequestration. The Bone Marrow Failure refers to the production of RBCs, WBCs, and platelets, which are reduced by the inhibition of hematopoietic stem cells, typical of aplastic anemia and marrow failure resulting from chemotherapy (Moore et al.,2023). Conversely, the Marrow Infiltration framework indicates that the replacement of normal marrow tissue by leukemia, lymphoma, and metastatic cancers through hematopoiesis is impaired. Nutritional deficiency, particularly a deficiency of vitamin B12 and folate, is the cause of ineffective hematopoiesis as well as abnormal DNA synthesis, which results in Megaloblastic pancytopenia. According to studies on megaloblastic anemia published between 2022 and 2025, megaloblastic anemia was found to be the primary cause in 40-72% of severe cases of pancytopenia in developing nations, with leukemia representing about 15-20% of severe cases (Schupp et al.,2024). There is also peripheral destruction, which is exacerbated by the way of hypersplenism and autoimmune disorders, in which the blood cells are prematurely destroyed. Most importantly, a key argument existing among researchers was that pancytopenia is not brought about by a single mechanism but that it is a multifaceted cooperation of the marrow dysfunction, immune responses, and processes of systemic diseases.

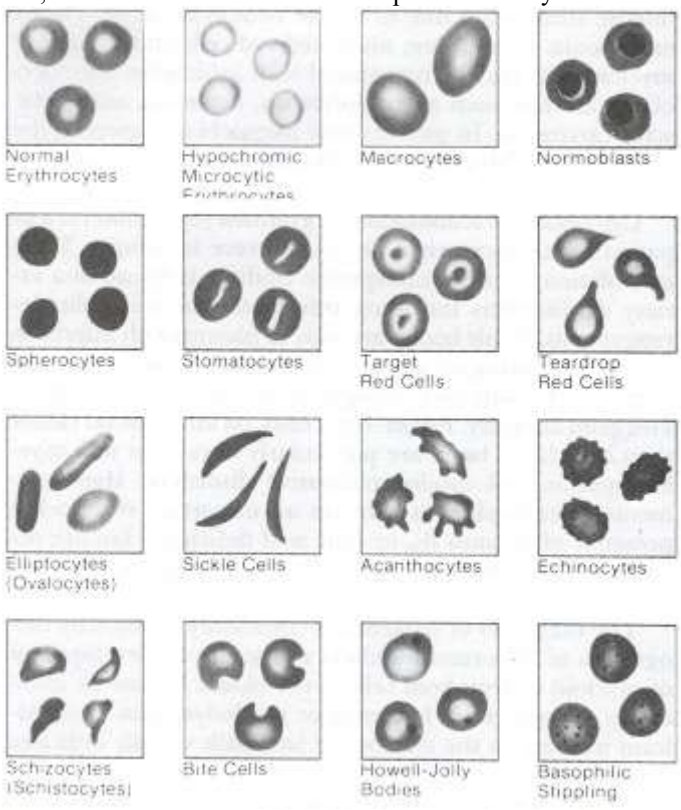

Figure 2: Components Seen in Peripheral Smear

(Source: https://www.ncbi.nlm.nih.gov/books/NBK263/)

Peripheral Smear Examination

Peripheral smear examination is a technique hematological method that is simpler and less expensive to conduct, and is utilized to determine the shape of blood cells. It is usually stained with the

Wright-Giemsa stain and examined under a microscope to determine the size and shape of the cells, the pattern of staining, and any abnormal inclusions. Bain (2023) mentioned smears are still important to identify blasts and dysplastic cells, whereas Chiravuri et al. (2023) pointed out the significance of smears in diagnosing early pancytopenia. Nevertheless, automated analyzers might overlook some minor morphological defects, and it is evident that microscopic analysis continues to offer better clinical interpretation in complex hematological cases.

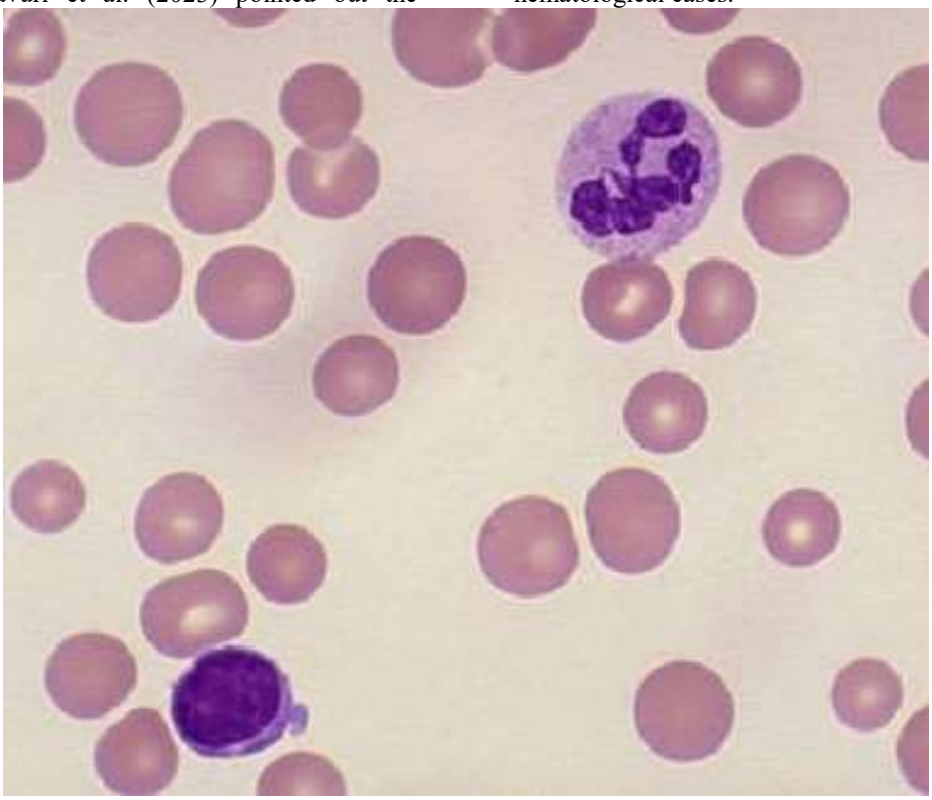

Figure 3: Megaloblastic anemia morphology
(Source: Killeen and Adil 2025)

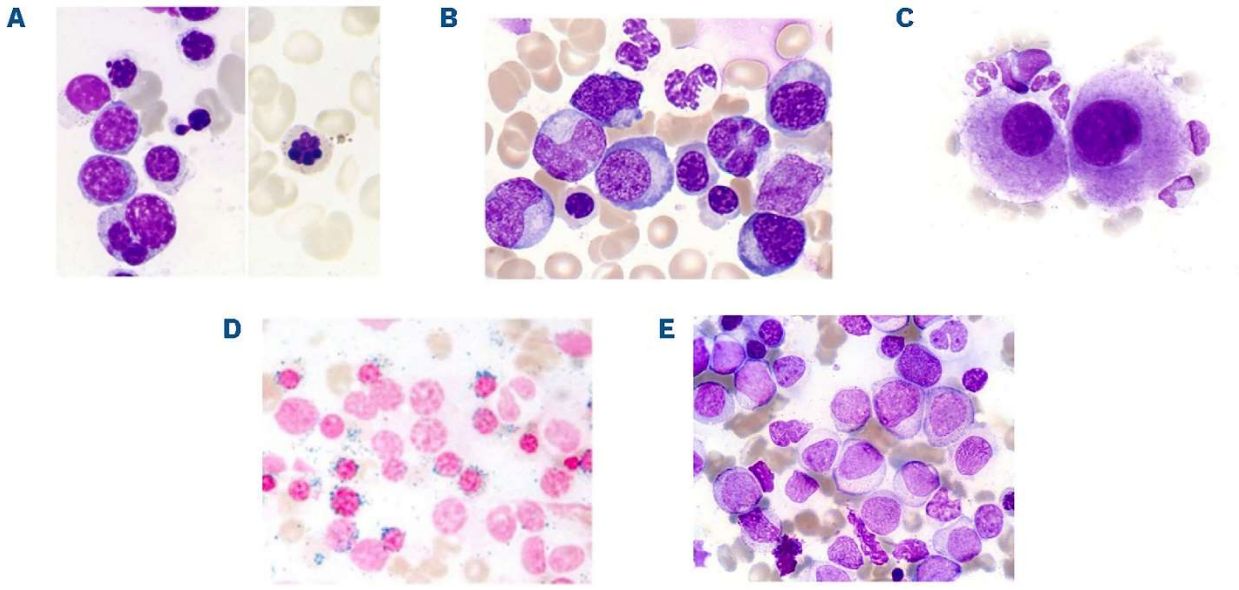

Figure 4: MDS dysplastic cells
(Source: https://haematologica.org/article/view/haematol.2023.284937)

Morphological Findings in Different Disorders

Morphological observation of a peripheral smear with regard to underlying pancytopenia is different and has significant diagnostic value. Xiao et al. (2022) revealed that macro-ovalocytes and hypersegmented neutrophils are typical manifestations of megaloblastic anemia because of the failure of the DNA synthesis process, which in turn supports the ineffective theory of hematopoiesis. Conversely, Saheena et al. (2026) described cases of aplastic anemia with profound pancytopenia and significantly decreasing cellular elements due to bone marrow failure. Leukemia often shows the presence of circulating blast cells, whereas myelodysplastic syndrome is characterized by dysplastic neutrophils and abnormal nuclear segmentation. Other trials by Chen et al. (2023) also found reactive lymphocytes in viral diseases, but this could be confounded with early malignant diseases, which decreases diagnostic specificity. Altogether, the existing evidence indicates that peripheral smear interpretation is very valuable, but needs clinical correlation to guarantee accurate diagnosis (Mohammed et al.,2024).

Diagnostic Importance of Peripheral Smear

The peripheral smear examination can significantly contribute to the timely diagnosis of pancytopenia since blood cell morphology may be detected early, yet invasive procedures are carried out before the diagnostic test is performed. According to a study conducted by Sulardjaka et al. (2022), preliminary diagnosis was supported by results of the peripheral smear procedure in almost three-quarters of hematological disorders. Smear examination is more cost-effective, faster, and most importantly, more common, of course, compared with bone marrow biopsy, particularly in low-resource settings. Didehban et al. (2024) discuss that a peripheral smear would be a good guiding factor on the necessity of a bone marrow examination by revealing patterns of blasts, dysplastic cells, and severe cytopenia. Recently, reviews of studies also demonstrated its usefulness in distinguishing between megaloblastic anemia and leukemia and the effectiveness of the treatment procedure, monitored by cell morphology (Chen et al.,2023). However, a number of authors stressed that smear interpretation requires a great contribution of laboratory experience and clinical correlation in order to reduce the diagnostic effectiveness of complicated cases.

Literature Gap

Current research on pancytopenia is primarily concentrated on bone marrow pathology and laboratory parameters, but there is limited combined research done concerning the direct diagnostic significance of the morphology of peripheral smears. Research by Sulardjaka et al. (2022), Didehban et al. (2024), and Chen et al. (2023) showcased abnormal smear results but had minimal clinicopathological association. Moreover, the majority of the studies have been done in the tertiary centers, where there is a lack of emphasis on developing countries, where the advanced diagnostic facilities are not easily available also limited. There is also a lack of comparative analysis of smear results between various diseases in the existing literature, which leads to gaps in the diagnosis of the condition at an early stage and in the evidence-based use of hematological data.Conceptual Framework

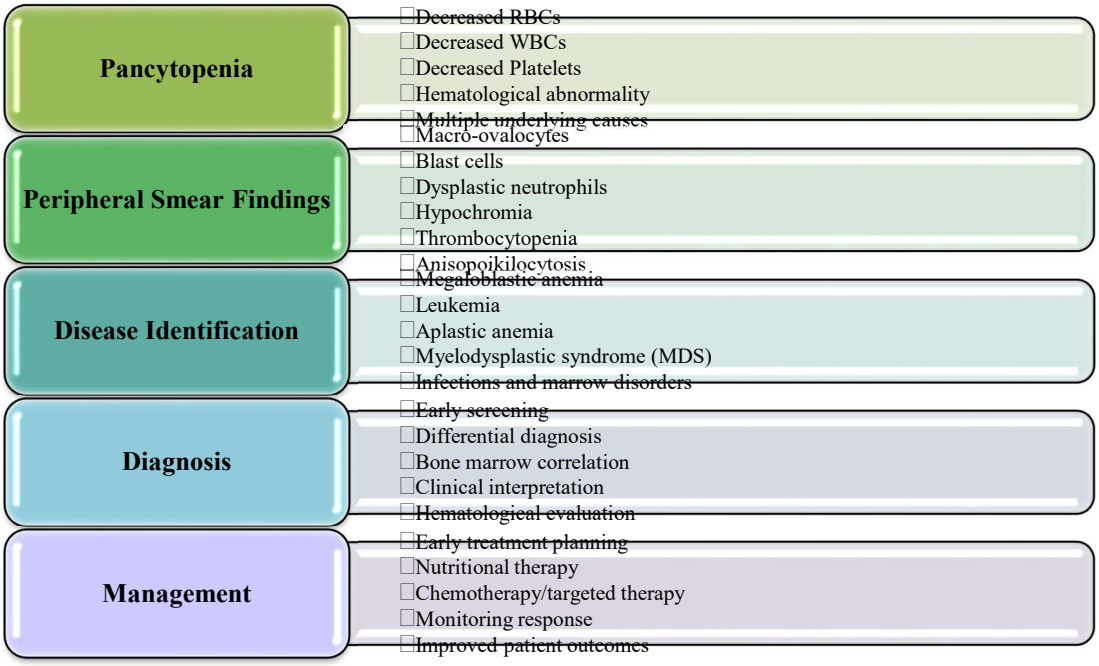

Figure 5: Conceptual Framework of Peripheral Smear Evaluation in Pancytopenia
(Source: Self-created)

Conclusion

The literature reviewed ensures that peripheral smear examination is a tool of diagnosis in the evaluation of pancytopenia that is still very important and cost-effective. Morphological examination will contribute to the aim of the study and research objectives because this method will help in early detection of the disease, provide direction in the future hematological examinations, and also enhance the accuracy of diagnosis analysis in combination with the clinical results.

Methodology

Research Approach

In this study, a qualitative descriptive research approach was employed to assess the peripheral smear observations in pancytopenia. This was a suitable approach as it assisted in the explanation of morphological patterns, the association of the disease, and diagnostic significance using in-depth analysis of the available evidence (Patel et al.,2025). Compared to the quantitative approach, the qualitative approach has enabled critically comparing the hematological results in various disorders and enabled a more profound perception of the problem of diagnosis of pancytopenia.

Research Design

Literature-based review research design was employed to conduct a review of literature concerning published literature on peripheral smear and pancytopenia. The design was beneficial to the research objective as it enabled comparison of the recent clinical studies, hematological theories, and diagnostic practices (Qiao et al.,2022). The design of the review also contributed to identifying similarities, differences, and gaps in the previous studies, which enhanced the influence of critical evaluation of peripheral smear interpretation in various hematological disorders.

Research Method

The research mainly utilized secondary data sources, such as peer-reviewed journals, hematology textbooks, PubMed articles, WHO publications, Springer, and MDPI databases, all published from 2021 to 2026. The use of secondary research was based on the principle that it has access to up-to-date clinical evidence and extensive hematological research (Amonoo et al.,2022). This was more appropriate than primary data collection in terms of synthesizing the current diagnostic knowledge, assessment of various disease conditions, and comparing peripheral smear findings in various patient populations.

Data Collection

Keywords used to gather relevant literature include pancytopenia, peripheral smear, hematological disorders, bone marrow failure, and morphological abnormalities. Articles have been chosen according to their relevance, date of publication, and scientific authenticity. The emphasis was put on open-access medical studies and recent reviews of hematology (Leng et al.,2025). This methodological systematic search design enhanced consistency and adherence to

the research objectives, diagnostic emphasis, and research study questions.

Research Ethics

The study upheld academic integrity through the application of credible academic sources used in the study and in-text citation skills. A critical rephrasing of all information was done to prevent plagiarism and guarantee originality (Muthanna et al.,2024). There was no use of patient data or any confidential data since the study relied solely on secondary published sources and publicly available medical research evidence.

Results & Findings

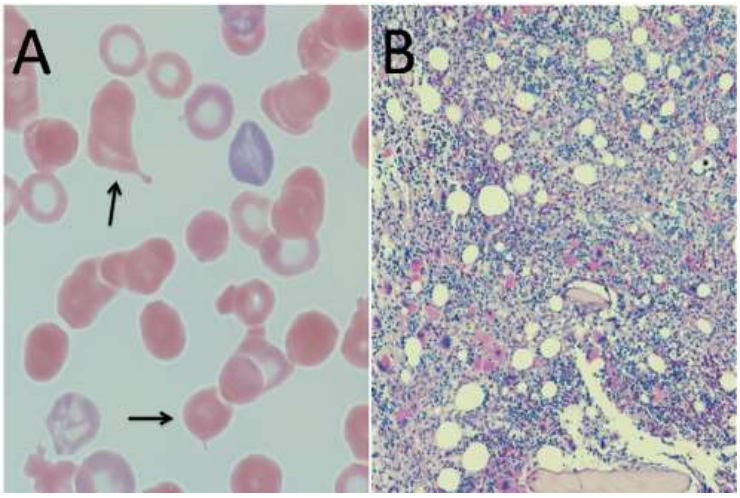

Figure 6: Common Smear Findings in Pancytopenia

(Source: https://www.researchgate.net/figure/A-Peripheral-blood-smear-reveals-moderate-anisopoikilocytosis-with-some-tear-drop-cells_fig1_265250193)

Common Peripheral Smear Findings

The analyzed literature demonstrated that the results of the peripheral smear have a significant role in diagnosing the cause of pancytopenia. Chiravuri and De Jesus (2023) reported that anisopoikilocytosis and hypochromia are commonly associated with nutritional anemia and ineffective erythropoiesis. Similarly, Killeen and Adil (2025) found that a key finding in megaloblastic anemia is the existence of macrocytosis when it is as a result of vitamin B12 and folate deficiency. Correspondingly, thrombocytopenia and a lowering of cellular elements were examined in aplastic anemia (Bhuyan et al., 2022), whereas the presence of circulating cells in the form of blast cells was used as a strong sign of leukemia and disorders of the marrow's infiltration (Chew and Kamangar, 2024). Lendrum et al. (2024) critically remarked that not all morphological changes are distinctly benign or malignant, and a peripheral smear alone will not enable any diagnosis without clinical and bone marrow confirmations.

Correlation Between Smear Findings and Diseases

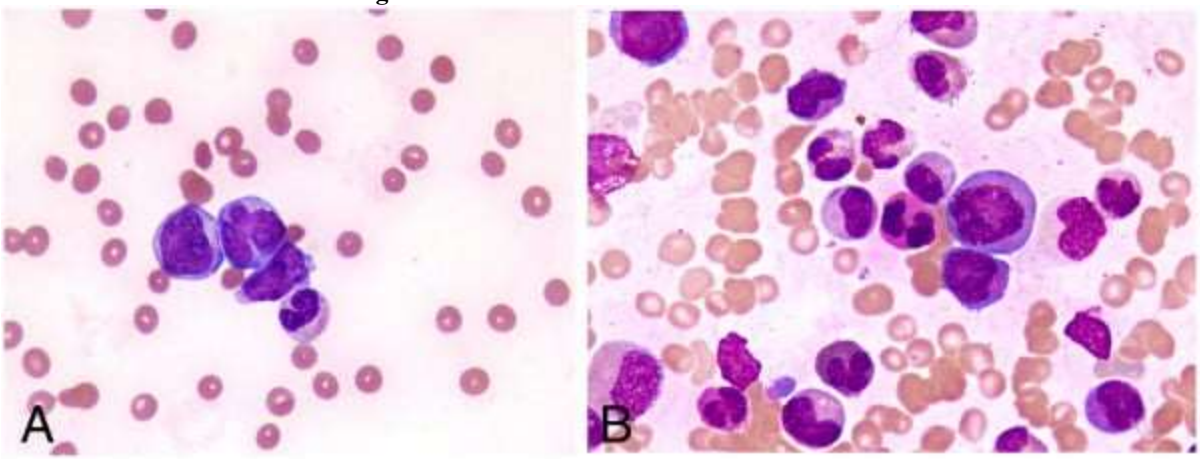

Figure 7: Correlation Between Peripheral Smear and Bone Marrow

(Source: https://www.researchgate.net/figure/Peripheral-blood-smear-and-bone-marrow-aspirate-A-Peripheral-blood-smear-showing-blast_fig2_255788503)

Research revealed that peripheral smear results were highly positive associations with particular hematological conditions. According to Killeen and Adil (2025), macro-ovalocytes are typical characteristics of a megaloblastic anemia that develops due to inhibited DNA synthesis. According to Chew and Kamangar (2024), circulating blast cells were found to be a significant predictor of leukemia and marrow infiltration. The common symptom articulated by (Niddk.nih.gov, 2020) of aplastic anemia is that it is characterized by significantly reduced formed elements because of bone marrow failure. Oster et al. (2024) and Besa (2024) focused on the dysplastic neutrophils and the abnormal nuclear morphology in MDS. But the morphological overlap between aplastic anemia and MDS might diminish diagnostic specificity, showing the relevance of a combination of the smear interpretation with clinical and bone marrow analysis.

Disease	**Smear Finding**
Megaloblastic anemia	Macro-ovalocytes
Leukemia	Blast cells
Aplastic anemia	Reduced formed elements
MDS	Dysplastic cells

Table 2: Disease &Smear Finding
(Source: Self-created)

Diagnostic Role of Peripheral Smear

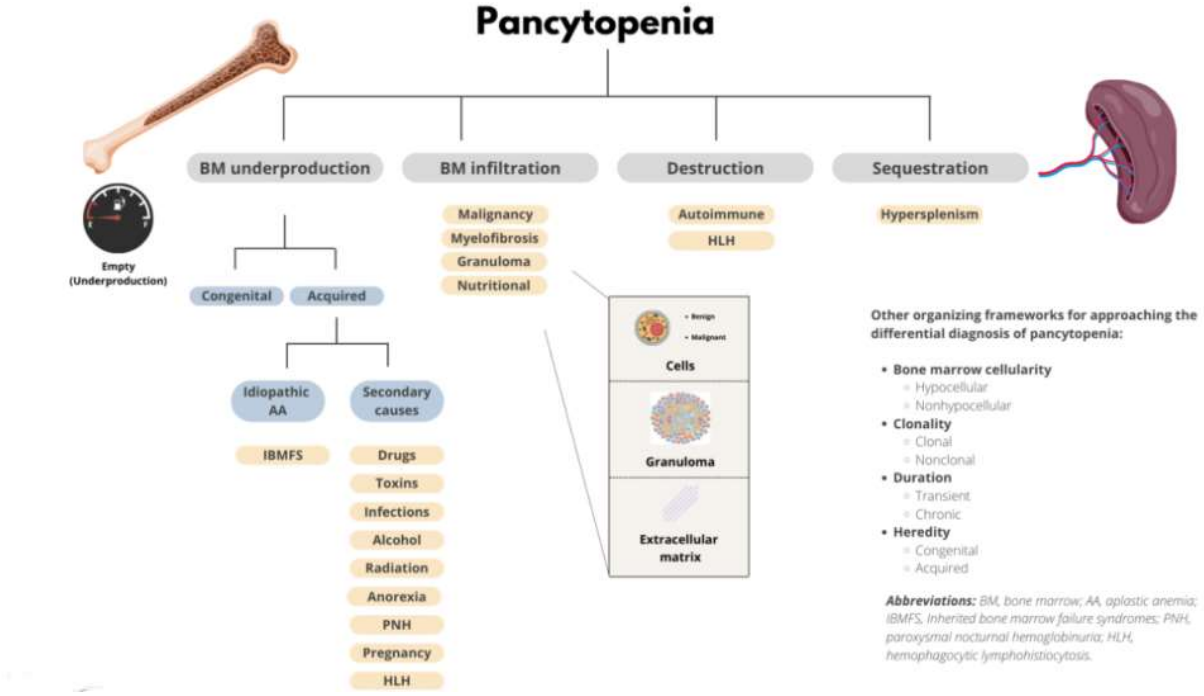

Figure 8: Diagnostic Approach to Pancytopenia
(Source: https://www.thebloodproject.com/pancytopenia/)

The results revealed that the peripheral smear analysis is highly suitable for initial screening and analysis of pancytopenia. As Chew and Kamangar (2024)

highlighted, smear analysis is the fastest source of morphological evidence that enables clinicians to consider nutritional anemia, leukemia, infections, and marrow failure diseases prior to the adoption of invasive procedures. Equally, Chiravuri and De Jesus (2023) indicated that abnormal cells like blasts, macro-ovalocytes, and dysplastic neutrophils assist in early differentiation diagnosis and direct further investigations into their classification. Chonat et al. (2023) critically observed that microscopic smear analysis is an effective method compared to automated analyzers to identify minor morphological abnormalities. Additionally, Patel et al. (2025) and Bhuyan et al. (2022) reviewed that peripheral smear results can be used to identify the need to take a bone marrow biopsy, especially when the cytopenia is not clearly explained and suspected malignant disorders are present. However, a number of studies pointed out that overlapping morphological patterns can diminish the diagnostic specificity. Thus, the use of peripheral smear in the diagnosis of pulmonary embolism should be used in conjunction with clinical data and bone marrow to enhance diagnostic validity and assist in appropriate patient care.

Challenges and Limitations

These results demonstrated that there were a number of limitations to the application of peripheral smear examination to diagnose pancytopenia. Observer variability is one of the greatest challenges, as the same can be interpreted differently depending on the experience and expertise of the hematologist. According to Chew and Kamangar (2024), minor abnormalities like dysplastic neutrophils or early blast cells may sometimes not be noticed when microscopic observations are conducted regularly through evaluation. Equally, Chonat et al (2023) observed that manual interpretation of smears relies heavily on expert observation, which decreases the consistency of smear interpretation across laboratories. The other significant limitation is the lack of a clear distinction between various hematological conditions in terms of their morphology. For example, both megaloblastic anemia and myelodysplastic syndrome may exhibit macrocytosis, whereas aplastic anemia and diseases of marrow infiltration may be associated with pancytopenia with decreased cellular components. Bhuyan et al. (2022) highlighted those similarities complicate the process of conducting a differential diagnosis and postponing the proper treatment. Even though peripheral smear is still useful when it comes to early screening and the ability to achieve the study objectives, there is evidence to indicate that it is not capable of making conclusions on diagnosis in complex cases. Thus, the diagnostic accuracy can be enhanced via expert interpretation, correlation with clinical considerations, and bone marrow analysis in order to minimize misdiagnosis and provide effective management of the patients in the context of the pancytopenia assessment.

Discussion

Advantages	Limitations
Low-cost	Observer variability
Rapid diagnosis	Overlapping morphology
Accessible	Requires expertise
Early screening	Cannot confirm diagnosis alone

Table 3: Advantages and Limitations of Peripheral Smear

(Source: Self-created)

The results of the current study are supported by the previous studies that have indicated that peripheral smear examination is still a valuable initial investigation in the examination of pancytopenia. Similar outcomes were obtained in other studies by Chew and Kamangar (2024) and Chiravuri and De Jesus (2023), following a rapid diagnostic clue is report by smear morphology before invasive procedures are conducted. The recent results have found macro-ovalocytes and hypersegmented neutrophils to be typical of megaloblastic anemia, which concurs with Killeen and Adil (2025), who associated the abnormalities with impaired DNA production and inefficient hematopoiesis. In comparison to leukemia and myelodysplastic syndrome, megaloblastic anemia exhibits more typical morphological alterations, and thus, smear analysis can be used clinically to make an early differential diagnosis.

The study also indicates the value of the practical usefulness of a peripheral smear examination in the resource-restricted environment where an elucidate diagnostic center and bone marrow biopsy could not be instantly provided. Bhuyan et al. (2022) discussed that the use of peripheral smear analysis may aid in minimizing irrelevant invasive practice and aid in a prompt medical decision-making process. However, significant limitations were found in the results as well. The morphological overlaps between aplastic anemia, myelodysplastic syndrome, and leukemia can decrease diagnostic specificity and promote observer variability. Thus, the diagnosis cannot be made in all cases by the means of peripheral smear alone.

Overall, the findings indicate that the study's aim and objectives are supported since they demonstrate that peripheral smear analysis enhances early screening,

distinction of the disease, and directs bone marrow analysis in conjunction with clinical examination and lab results.

Conclusion

In conclusion, the peripheral smear examination is a tool of pivotal importance, which in the evaluation of pancytopenia is both relevant and affordable. The results of the study indicated that smear morphology aids in the detection of diseases at early stages, the distinction between the diseases, and the identification of underlying hematological diseases. Though a peripheral smear offers valuable diagnostic clues, to secure a correct diagnosis, it has to be combined with clinical evidence and examination of bone marrow. All in all, the research was able to meet its aims and objectives because it had to clearly clarify how peripheral smear plays a critical role in enhancing diagnostic assessment and patient care in pancytopenia.

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