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Original article

THE ROLE OF ABSOLUTE RETICULOCYTE COUNTS IN EVALUATION OF PANCYTOPENIA: A CROSS-SECTIONAL STUDY, BIHAR, INDIA.

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Abstract

Background

Hematological conditions like pancytopenia are widespread in our lab. Diagnosis and therapy of pancytopenia require etiology analysis. Most pancytopenia causes are determined by the Absolute Reticulocyte Count (ARC), which has been neglected. The aim of this study is to determine the importance of the Absolute Reticulocyte Count (ARC) in assessing the etiology of pancytopenia, with a focus on its role in distinguishing between different causes of this hematological condition.

Materials and Methods

The study was conducted in a tertiary health care institution in Bihar, India. Over the course of 1 year (April 2021 to March 2022), a descriptive cross-sectional study was carried out. Complete blood counts (CBC), reticulocyte count including ARC and peripheral blood smear (PBS) examination were performed in all cases of pancytopenia. Serum ferritin, Serum vitamin B12 level and serum folate were also estimated. Bone marrow examination was done in all cases.

Results

A total of 200 pancytopenia cases were assessed, and the findings were recorded. In cases of aplastic anemia, ARC was found to be $<25x10^9$ /L, in megaloblastic anemia ARC was found to be $25\text{-}50x10^9$ /L and ARC $>100x10^9$ /L was seen in neoplastic disorders. Lower ARC values were associated with conditions like aplastic anemia, while higher ARC values were indicative of acute leukemia and metastatic deposits, making ARC a valuable diagnostic tool.

Conclusion

It was concluded that ARC is crucial in distinguishing between different causes of pancytopenia, and it must be a regular part of work-up to prevent needless invasive bone marrow examinations in cases of pancytopenia.

Recommendation

This study suggests that pancytopenia patients be routinely assessed with Absolute Reticulocyte Count (ARC). ARC helps identify pancytopenia etiologies, preventing needless bone marrow exams. Pancytopenia diagnosis and treatment can be improved by adding ARC to diagnostic techniques.

Keywords: Bone marrow aspiration, Absolute reticulocyte count, Aplastic anemia, Reticulocyte percentage, Pancytopenia
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Introduction

Pancytopenia characterized by reduced counts of red blood cells, white blood cells and platelets, is a hematological condition resulting from various underlying disease processes, mostly involving the bone marrow.

Accurately diagnosis the cause of pancytopenia requires a systematic approach, and reticulocyte counts are invaluable in this process [1]. Reticulocyte parameters including reticulocyte percentage, absolute reticulocyte count, mean reticulocyte volume (MRV), and immature reticulocyte fraction (IRV) play a crucial role in assessing hematologic diseases and monitoring patients undergoing different therapies [2].

Hematology analyzers have made it easier to count and assess the maturity of reticulocytes, providing precise data on the age distribution of reticulocyte populations. This automated evaluation eliminates subjectivity and technical variability associated with manual counting, making it cost-effective for analyzing a large number of samples [2, 3]. Newer reticulocyte indices offer valuable insights into marrow erythropoietic activity, making them particularly useful in evaluating pancytopenia.[4]

Reticulocyte count (percentage) reflects the rate of red blood cell turnover, with a normal range of 1%-2% indicating the daily replacement of circulating red blood cells [1].

Immature reticulocyte fraction (IRF) represents the least mature fraction of reticulocytes, offering an early and sensitive measure of bone marrow erythropoietic activity. This parameter aids in classifying anemias based on erythropoietic response and typically falls within the range of 0.11-0.38 [4, 5]. Recovery of bone marrow after bone marrow transplantation, following therapy with erythropoiesis stimulating drug or chemotherapy is shown by increased IRF within a few days. [6]

Mean reticulocyte volume (MRV), approximately 24% higher than the mean cell volume (MCV) of mature erythrocytes, provides a "hematocrit" value for reticulocytes. Monitoring treatment response and serving as a sensitive marker of erythropoiesis are among its key functions [6]. In contrast to invasive bone marrow aspirations or costly biochemical tests, reticulocyte indices offer a non-invasive and cost-effective means of identifying the underlying cause of pancytopenia, making them a valuable tool in clinical practice [7,8].

Reticulocyte haemoglobin content (CHr) is an indicator of bone marrow iron status.[6]

Absolute reticulocyte count (ARC) is a marker for assessing red cell production. It is calculated by multiplying reticulocyte count/percentage with red blood cell count. Its normal value is 50-100x10^9 /L. The present study conducted an assessment of ARC in individuals presenting with pancytopenia.

Materials and Methods

Study design:

A descriptive cross-sectional study was carried out.

Study setting:

This study was carried out at the Hematology department of Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India, over the course of 1 year (April 2021 to March 2022).

Participants:

The analysis was conducted on 200 cases of pancytopenia.

Inclusion criteria:

Patients of pancytopenia, characterized by hemoglobin levels <10g/dl, WBC counts <4000/µl, and platelet counts <1,00,000/µl, detected on routine complete blood counts.

Exclusion criteria:

All patients previously diagnosed with pancytopenia. Patients who have undergone recent blood transfusion or have a history of prior chemotherapy or radiotherapy

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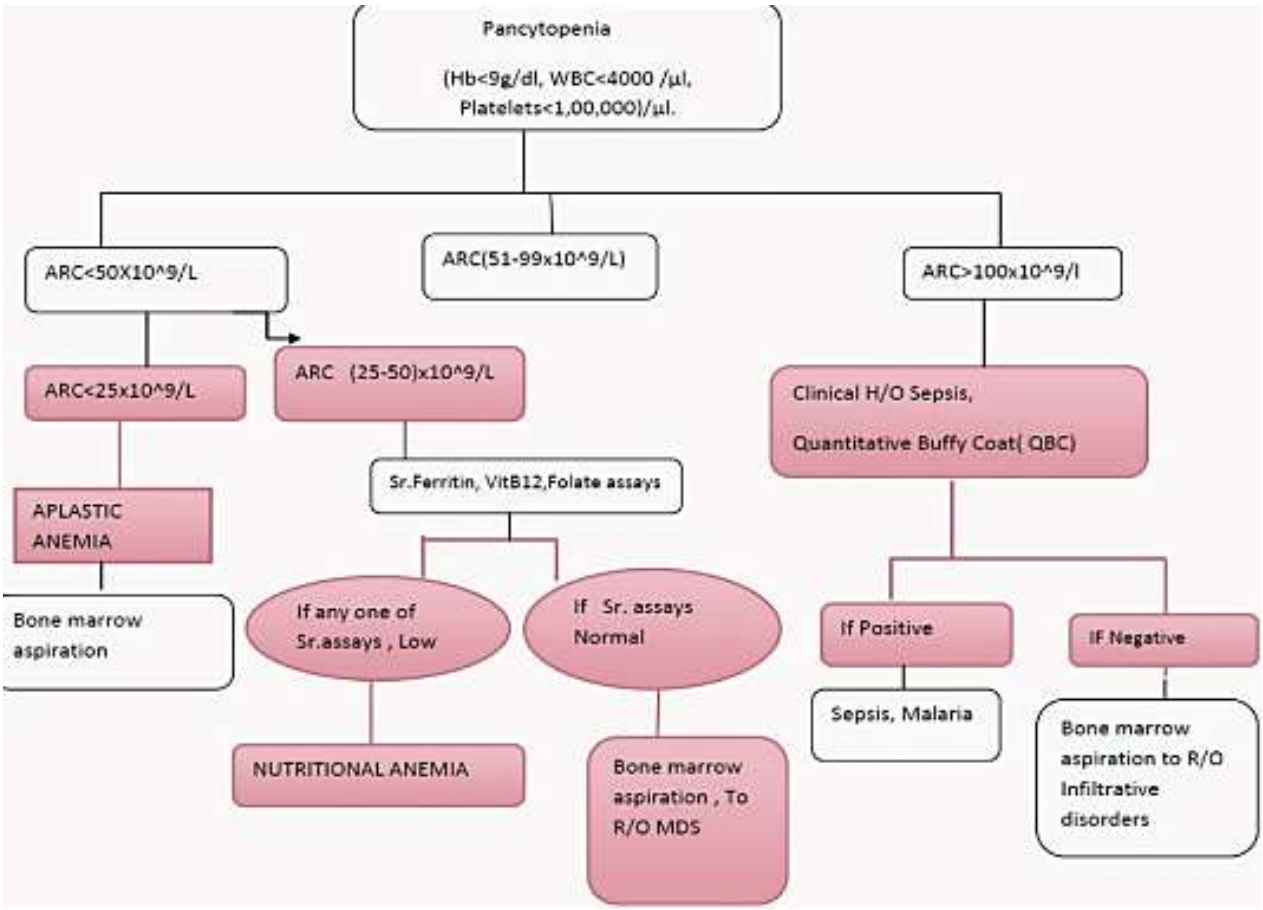

Figure 1: An Algorithm to approach cases of pancytopenia

Data Collection and Analysis:

Comprehensive clinical data was meticulously gathered from the subjects. Routine hemogram was performed on fully automated Hematology analyzer, examination of the peripheral blood smear stained with Leishman's stain, assessment of the reticulocyte count and ARC by automated method was done. Furthermore, serum assays for vitamin B12, serum folate, and serum ferritin were conducted on all cases. Bone marrow examination was performed for all subjects.

Bias:

There was a chance that bias would arise when the study first started, but we avoided it by giving all participants the identical information and hiding the group allocation from the nurses who collected the data.

Ethical considerations:

The study protocol was approved from the review and ethics committee and written informed consent was received from all the participants prior to the investigation. The ethical aspects of the research were carefully thought out to preserve patient privacy and confidentiality.

Statistical analysis

The data evaluation was performed using SPSS Version 15.0. The mean and standard deviation were calculated for the parameters related to hematology in each case.

Results

A comprehensive analysis was conducted on 200 cases of pancytopenia. Notably, the distribution of gender revealed that 74.29% of the cases were attributed to the male population. The age range of the participants in the study spanned from 4 years to 81 years. Megaloblastic anemia emerged as the most prevalent etiology of pancytopenia, accounting for 57% of cases. Subsequently, aplastic anemia accounted for 28% of cases and acute leukemia for 8% of cases. Myelodysplastic syndrome and multiple myeloma accounted for 2% cases each. Kala-azar and metastatic deposits accounted for 1.5% cases each.

Table 1: Clinical presentation of pancytopenia

Clinical finding	Percentage
Pallor	100
Weakness	67
Fever	44
Splenomegaly	29
Hepatomegaly	21
Pain abdomen	24
Bleeding	17
Dyspnea	17
Weight loss	17
Lymphadenopathy	14
Icterus	12
Bone pain	07
Other (Decrease appetite, diarrhea, vomiting)	14

Table 2: Mean reticulocyte count and Mean ARC

S. No.	Causes	No. of cases (%)	Reticulocyte count (%)	Absolute reticulocyte count (x 10^9/L)
1.	Megaloblastic Anemia	57	0.100	40.74
2.	Aplastic Anemia	28	0.100	21.19
3.	Acute Leukemia	8	3.516	130.30
4.	Myelodysplastic Syndrome	2	0.100	32.50
5.	Multiple Myeloma	2	0.100	10.82
6.	Kala-azar	1.5	0.100	12.31
7.	Metastatic Deposits	1.5	4.500	186.10

Table 2 represents the etiology of pancytopenia with percentage of cases, mean reticulocyte count and mean ARC.

In megaloblastic anemia, mean ARC was 30.74 x10^9 /L. The ARC exhibited a significant reduction in patients diagnosed with Aplastic Anemia, demonstrating a mean value of 21.19x10^9 /L. In Myelodysplastic Syndrome, Multiple Myeloma and Kala-azar mean ARC was 32.5, 10.82 and 12.31 respectively however; it is noteworthy that the Mean Reticulocyte percentage remained consistent across all aforementioned cases, measuring at 0.1%. In cases of acute leukemia and metastatic deposits mean ARC was 130.30 and 186.10 respectively.

An interesting finding was that the Mean Reticulocyte percentage remained consistent across all these cases, measuring at 0.1%. In contrast, cases of acute leukemia and metastatic deposits exhibited significantly elevated ARC values, with mean ARC values of 130.30 and 186.10, respectively.

These results highlight the crucial role of ARC in distinguishing between different etiologies of pancytopenia. Lower ARC values were associated with conditions like aplastic anemia, while higher ARC values were indicative of acute leukemia and metastatic deposits. The consistent Mean Reticulocyte percentage across cases suggests that ARC provides a more specific indicator for assessing the underlying causes of pancytopenia, making it a valuable tool in clinical diagnosis and treatment decision-making.

Discussion

In this study, megaloblastic anemia emerged as the predominant cause of pancytopenia, constituting 57% of all pancytopenia cases with mean reticulocyte count of 0.1%. Aplastic or hypoplastic anemia constituted 28% of the pancytopenia cases observed in the study, exhibiting a mean reticulocyte count of 0.1%. Acute leukemia ranked as the third most prevalent cause of pancytopenia constituting 8% with mean Reticulocyte count of 3.5%.

These findings corroborate previous study by Khodke, which also identified megaloblastic anemia as the primary contributor to pancytopenia [9]. Similarly, in their 2016 study of 56 pancytopenia cases, Jella and Jella [10] reported megaloblastic anemia as the leading cause (42.9%), followed by aplastic anemia (23.2%). In a 2017 investigation of 40 pancytopenia cases, Shah et al. found megaloblastic anemia to be the most prevalent cause (35%), followed by aplastic anemia (32.5%), with additional cases involving acute leukemia, myelodysplastic syndrome (MDS), and round cell tumor [11]. Nevertheless, it is imperative to acknowledge that these findings are in stark contrast to studies conducted on a global scale. In the study conducted by Hossain et al., it was observed that aplastic anemia emerged as the predominant etiology of pancytopenia [12]. In a retrospective analysis encompassing a cohort of 48 individuals diagnosed with pancytopenia, Kumar et al. [13] observed that the predominant etiology was hypoplastic marrow, accounting for 33.33% of cases. The observed disparities can be ascribed to the elevated prevalence of nutritional anemia and severe malnutrition within the Indian population.

Various causes of pancytopenia had different absolute reticulocyte counts. Cases of Aplastic anemia had mean ARC of $21.19x10^9$ /L. This is in concordance with a study by Jiskani et al. in 2018 mean ARC in aplastic anemia cases was $19.29\pm1.41x10^9$ /L [14]. Also, in a study by Priya et al. the mean ARC in aplastic anemia was $<25x10^9$ /L [1].

Cases of megaloblastic anemia had mean ARC of $40.74x10^9$ /L. In a study by Jiskani et al. in 2018 mean ARC in megaloblastic anemia cases was $54.21\pm1.32x10^9$ /L [14]. Also, in a study by Priya et al. the mean ARC in megaloblastic anemia was $25\text{-}50x10^9$ /L [1].

Cases of leukemia and metastasis had mean ARC of $130x10^9$ /L and $186x10^9$ /L respectively. In the study by Jiskani et al. in 2018 mean ARC in leukemia and metastasis cases was $85.38\pm1.58x10^9$ /L and $141.81\pm2.55x10^9$ /L [14]. Also, in the study by Priya et al. the mean ARC in infiltrative disorders was $>100x10^9$ /L [1].

Conclusion

The present study underscores the significance of employing a systematic approach in instances of pancytopenia, as it is imperative in order to circumvent superfluous invasive measures such as bone marrow aspiration. The superiority of ARC in distinguishing hypoproliferative anemias from hyperproliferative anemias was observed.

Limitations:

The limitations of this study include a small sample population who were included in this study. The findings of this study cannot be generalized for a larger sample population. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendation:

Based on the findings of this study, we recommend that healthcare practitioners include Absolute Reticulocyte Count (ARC) as a routine component in the assessment of pancytopenia cases. ARC plays a vital role in distinguishing between various etiologies of pancytopenia, helping to avoid unnecessary invasive bone marrow examinations. Incorporating ARC into diagnostic protocols can enhance the accuracy and efficiency of pancytopenia diagnosis and subsequent patient care.

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List of abbreviations:

ARC- Absolute Reticulocyte Count
CBC- Complete blood counts
PBS- Peripheral Blood Smear
MRV- Mean Reticulocyte Volume
IRV- Immature Reticulocyte Fraction
IRF- Immature reticulocyte fraction
MCV- Mean Cell Volume

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The study was not funded

Conflict of interest:

The authors report no conflicts of interest in this work.

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