Research Article

Correlation of Peripheral Blood Findings with Bone Marrow Examinations in Patients with Unexplained Pancytopenia

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Abstract

Background: Pancytopenia of unknown cause can be a difficult problem in differential diagnosis due to possible connections between peripheral blood abnormalities, nutrient deficiencies, failure of the marrow and tumour diseases of the haematology specialty. This paper describes an approach to compare peripheral blood abnormalities against marrow diagnosis in terms of associations**.**

Method: An analysis was performed on 100 adult records retrospectively. The variables included demographics, clinical symptoms, blood measurements, peripheral smear morphology observations, marrow cellularity percentages, and marrow diagnoses. Summary descriptive statistics described the dataset. Associations were identified using Spearman correlation and Kruskal-Wallis rank sum test for cellularity correlation, and permutations testing correlations between categories. Percent agreement and Cohen's kappa coefficient measured agreement in diagnostic classification between peripheral findings and marrow examinations**.**

Results: The average age was 48.72 ± 19.10, with 52 percent women. Megaloblastic anaemia represented 34 percent diagnoses. Other diagnoses include aplastic anaemia (24%), acute leukaemia (16%), myelodysplasia (12%), infiltration (8%) and reactive/miscellaneous (6%). Morphological abnormalities included macrocytic erythrocytes (46), hypersegmented neutrophils (28), blast cells (14) and dysplasias (16). There were positive correlations for leucocytes ($\rho=0.380$; $p<0.001$) and thrombocytes ($\rho=0.381$; $p<0.001$) with cellularity. No correlation for haemoglobin existed ($p=0.1165$). Diagnostic agreement was high at 79%, with kappa coefficient $\kappa=0.729$**.**

Conclusions: This paper demonstrates how peripheral morphology, blood measurements and diagnoses might be combined into an analytic framework. Given the retrospective nature of the sample, no causal or diagnostic validity is implied here. Further prospective research is essential before any conclusion can be reached regarding clinical applications to cases of unexplained pancytopenia.

Keywords: Pancytopenia; Peripheral blood smear; Bone marrow examination; Marrow cellularity; Diagnostic agreement.

1. INTRODUCTION

Pancytopenia refers to reduced haemoglobin, leukocytes and platelets in the bloodstream concurrently. Clinically relevant, pancytopenia stems from various origins and results in weak patients that look pale, feverish, have recurrent infections or suffer bleedings due to nutritional deficiency, marrow failure or blood cancer (Kumar & Kumar, 2024). Gayathri and Rao found that analysis of peripheral blood and marrow aspirates helped discriminate highly different pathologies from cases showing identical profiles of cytopenias in pancytopenic patients [1]. Systematic exploration of pancytopenia therefore becomes necessary, and not merely labelling of one diagnostic category. Population-specific distributions matter here too, since Jain and Naniwadekar identified hypersplenism, infections, marrow toxicity, and megaloblastosis as leading causes among 250 participants prospectively recruited (Jain & Naniwadekar, 2026). Conversely, Patel and Prajapati discovered that the major cause of hospital admission was acute leukaemia, followed by megaloblastic anaemia and aplastic anaemia, among 546 adult cases visiting specialised haematology clinics [3]. Both studies provide context-dependant insight for the selection of diagnostic tests according to history and basic examination.

Basic blood testing consists in measuring complete blood counts, RBC indices, white cell differentials, and the inspection of peripheral smear. Blood findings like increased red cell size (macrocytosis), hypersegmented neutrophils, presence of blast cells, and abnormal leukocyte forms hint at certain specific diagnoses and guide additional tests. Dasgupta et al. described occurrence of hypersegmented neutrophils in some of the patients with megaloblastic anaemia [4]. However, despite the usefulness, morphological abnormalities fail to be universally identifiable, let alone specific for certain blood disorders. Safaei et al. showed that identification of circulating blasts

sometimes required bone marrow sampling despite being detected in peripheral blood, alongside cytogenetic analysis for certain cases [5]. Peripheral blood examination gives directions, but should be interpreted along with clinical information and marrow diagnosis.

Aspirates yield details on cellular structure, differentiation stages and abnormal populations, whereas biopsy allows for estimation of overall cellularity, histological structure, presence of fibrosis and infiltration. Studies of Desalphine et al. confirmed complementarity of both procedures and importance of biopsy in case of non-diagnostic aspirations – the dry or bloody tap results, inadequate sample material [6]. Likewise, Metikurke et al. found that marrow biopsy provided extra diagnostic information compared to bone marrow aspirate examination alone, stressing importance of using all three techniques [7]. Those studies suggest a possible examination of correspondence between the diagnostic potential of peripheral smear findings and bone marrow diagnostics among pancytopenic patients requiring further investigations. This research design aims to discover useful peripheral blood characteristics, serious pathologies, and interpret marrow examination results.

1.1. Study Rationale and Objectives

1. To assess the correlation of peripheral blood counts and morphological findings with bone marrow aspiration and trephine biopsy findings in patients with unexplained pancytopenia.
2. To determine the underlying causes of unexplained pancytopenia and evaluate the diagnostic agreement between peripheral blood impressions and final bone marrow diagnoses.

2. Materials and Methods

This design is a cross-sectional observational study involving 100 patients admitted with unexplained pancytopenia consecutively. The inclusion criteria encompass hemoglobin <10g/dL, leukocytes <4x109/L, and platelets <100x109/L after inconclusive evaluation. The reasons for exclusion are known causes, active cytotoxic treatment, and unwillingness to participate under informed consent. Patient characteristics are recorded as presenting symptoms, medications used, dietary habits, medical conditions, and physical examinations (de Carvalho et al., 2024). Haematological examinations involve full blood counts, index parameters, reticulocytes, and peripheral smear for morphologies. Bone marrow studies investigate cellular morphologies, maturation patterns, blasts, abnormal morphologies, age-adjusted cellularity, fibrosis, and infiltrations. Supplementary testing may be conducted accordingly. Diagnosis synthesis involves all three elements: the history, bone marrow results and investigations, while peripheral blood opinions will be made ahead of the bone marrows being reported. Descriptive analyses: continuous data is described using means or medians. Categorical variables are represented by numbers and proportions. Relationships are determined through chi-squared/Fisher's exact tests and correlations via Spearman's coefficient. Concordance rates will be estimated through percentage agreement and Cohen's Kappa, with 95% confidence intervals calculated. Significant difference levels are determined as $p < 0.05$. Ethics clearance and informed consent will precede patient enrolment and privacy will be protected throughout the process.

3. Results

3.1. Demographic, Clinical, and Haematological Characteristics

The sample consisted of 100 observations, including 48 male (48.0%) and 52 female patients (52.0%). Age varied between 18 and 79 years, with a mean of 48.72 ± 19.10 years. The symptoms included fever (64.0%), splenomegaly (38.0%) and bleedings (25.0%). Clinical signs were not mutually exclusive. Mean hemoglobin was 6.90 ± 1.06 g/dL (range, 4.10–9.70 g/dL). White blood cell means came out as 2.42 ± 0.77 × 10^9/L, and platelets as 53.79 ± 20.55 × 10^9/L. The mean corpuscular volume amounted to 98.87 ± 11.57 fL (range, 77.60 to 122.20 fL). Reticulocytes ranged from 0.10 to 1.83 percent, giving a mean of 0.64 ± 0.35 percent. Every observation satisfied pancytopenia threshold requirements established by numerical criteria in advance. Characteristics of demographic variables, reported signs and peripheral blood measurements were summarised in Table 1.

Table 1. Demographic characteristics, clinical features, and peripheral blood parameters in the Study dataset

(n = 100).

Characteristic	n (%) or mean ± SD	Range
Age, years	48.72 ± 19.10	18–79
Male	48 (48.0)	—
Female	52 (52.0)	—
Fever	64 (64.0)	—
Splenomegaly	38 (38.0)	—
Bleeding manifestations	25 (25.0)	—
Haemoglobin, g/dL	6.90 ± 1.06	4.10–9.70
Leukocytes, × 10^9/L	2.42 ± 0.77	0.69–3.90
Platelets, × 10^9/L	53.79 ± 20.55	8–96
Mean corpuscular volume, fL	98.87 ± 11.57	77.60–122.20
Reticulocytes, %	0.64 ± 0.35	0.10–1.83

3.2. Peripheral Blood Morphology and Bone Marrow Diagnoses

A large proportion of the diagnoses is megaloblastic anaemia, represented by 34 cases (34.0%). This is followed by aplastic anaemia (24 cases, 24.0%), acute leukaemia (16 cases, 16.0%) and myelodysplastic neoplasm (12 cases, 12.0%). Other categories are marrow infiltration (eight cases, 8.0%) and miscellaneous or reactive disorders (six cases, 6.0%). Diagnostic frequencies are shown in Figure 1. Morphology of normocytes was seen in 48 cases, of macrocytes in 46 and of microcytes in six cases. Of 34 cases with megaloblastic anaemia, 31 showed macrocytes. Similarly, of 12 cases with myelodysplasia neoplasm, nine had macrocytes. Hypersegmented neutrophils were seen in 28 cases, among which 25 cases were megaloblastic anaemia. Blast forms were seen in 14 cases, among which 12 cases were acute leukaemia and remaining two were myelodysplastic neoplasm. Of 16 cases with dysplastic blood cells, 10 were myelodysplastic neoplasm. Associations between blood and bone marrow diagnoses are reported in Table 2.

Table 2. Peripheral blood morphological findings according to final marrow diagnosis in the example dataset.

Peripheral blood finding	Megaloblastic anaemia	Aplastic anaemia	Acute leukaemia	Myelodysplastic neoplasm	Marrow infiltration	Reactive/ other	Total
Number of records	34	24	16	12	8	6	100
Macrocytic morphology	31	3	1	9	1	1	46
Normocytic morphology	3	19	13	3	6	4	48
Microcytic morphology	0	2	2	0	1	1	6
Hypersegmented neutrophils	25	0	0	3	0	0	28
Circulating blasts	0	0	12	2	0	0	14
Dysplastic blood cells	3	0	3	10	0	0	16

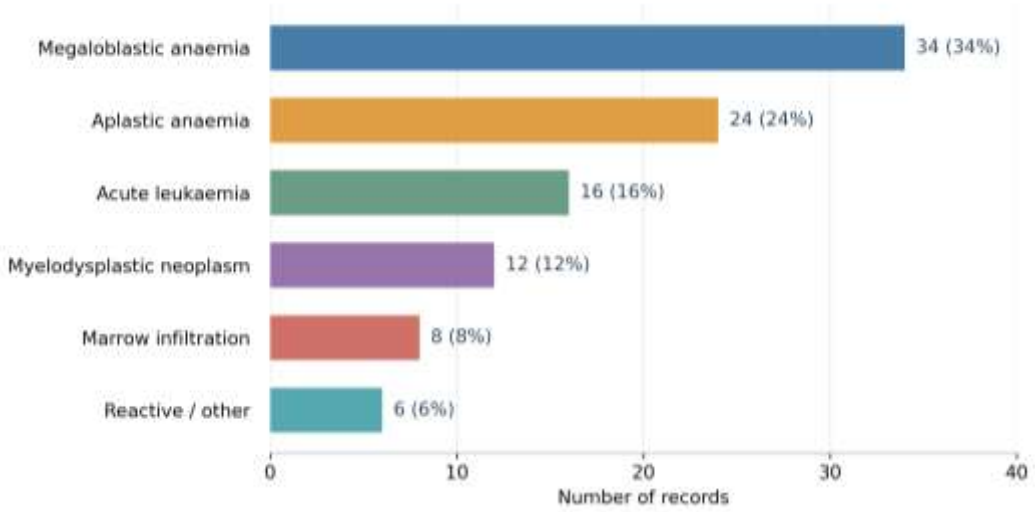


Figure 1. Distribution of underlying diagnoses assigned in the Study dataset(n = 100).

3.3. Association Between Peripheral Blood Parameters and Bone Marrow Findings

Cellularity of bone marrow biopsy samples was coded as hypocellular in 29 cases, normocellular in 15 cases, and hypercellular in 56 cases. The respective average leukocytes were 1.96, 2.51 and 2.63×109/L, while the respective averages platelets were 40.45, 58.13 and 59.54×109/L. These means can be visualised using Figure 2. Positive associations with cellularity category order existed both in terms of leukocytes and platelets. Their respective correlation coefficients were 0.380 and 0.381, and both were highly statistically significant at less than 0.001 probability level. MCV had the strongest association (ρ=0.447; p<0.001), followed by reticulocyte count (ρ=0.293; p=0.0031). Hemoglobin levels showed no correlation with cellularity (ρ=0.158; p=0.1165). The Kruskal-Wallis test confirmed significant differences among hypocellular, normocellular and hypercellular samples in terms of leukocytes, platelets, MCV and reticulocytes, but not hemoglobin (de Carvalho et al., 2024). In addition, exploratory permutation tests found positive associations with cellularity order in hypersegmentation, circulating blast and dysplasia.

Table 3. Associations between peripheral blood parameters, morphological features, and marrow cellularity in the example dataset.

Blood parameter	**Spearman ρ**	**p-value**	**Kruskal–Wallis H**	**p-value**
Haemoglobin	0.158	0.1165	3.458	0.1775
Leukocyte count	0.380	<0.001	16.293	<0.001
Platelet count	0.381	<0.001	17.492	<0.001
Mean corpuscular volume	0.447	<0.001	21.210	<0.001
Reticulocyte count	0.293	0.0031	12.939	0.0015
Morphological feature	**Pearson χ^2**	**Permutation p-value**		
Hypersegmented neutrophils	17.423	<0.001		
Circulating blasts	9.340	0.0105		
Dysplastic blood cells	6.896	0.0376		

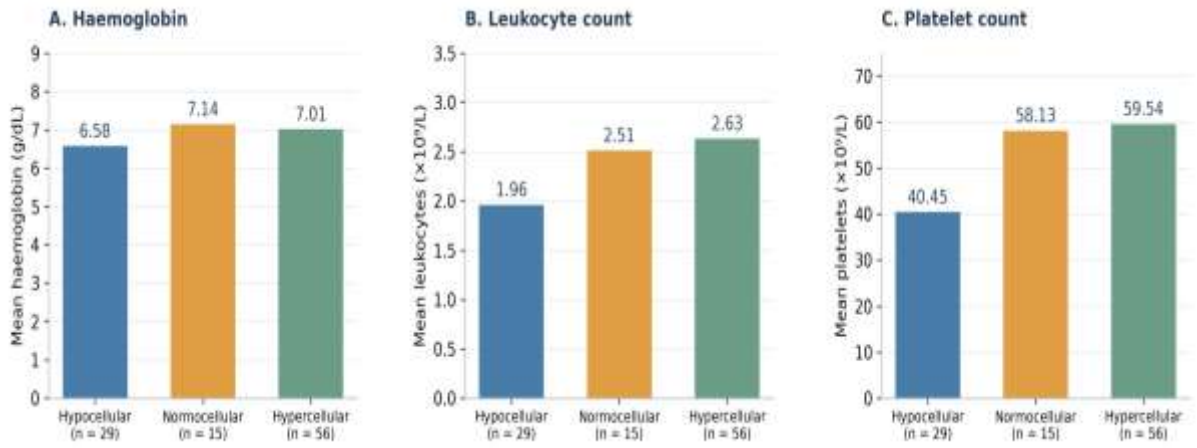


Figure 2. Mean haemoglobin, leukocyte count, and platelet count across marrow cellularity categories in the example dataset.

3.4. Diagnostic Agreement Between Peripheral Blood Impressions and Bone Marrow Diagnoses

Peripheral blood findings agreed with the final bone marrow diagnosis in 79 cases out of 100 observations, leading to a concordance of 79.0%. The agreement exceeded chance expectations by 22.5% and the Cohen's unweighted kappa coefficient was 0.729. Agreement can also be summarised using an agreement matrix where peripheral blood findings are listed across rows and final bone marrow diagnoses down columns, as seen in Figure 3. All observations categorised with final bone marrow diagnosis of megaloblastic anaemia showed corresponding peripheral blood finding agreement in 30 cases out of 34 (94.1%). Similarly, there were agreements in 21 observations out of 24 (87.5%) for aplastic anaemia and 14 observations out of 16 (87.5%) for acute leukaemia. Agreements were fewer for myelodysplastic neoplasm and marrow infiltrates (six cases out of 12, 50%; four cases out of eight, 50%, respectively). Reactive or other diseases showed agreement in four out of six observations (66.7%). One observation was classified as inconclusive.

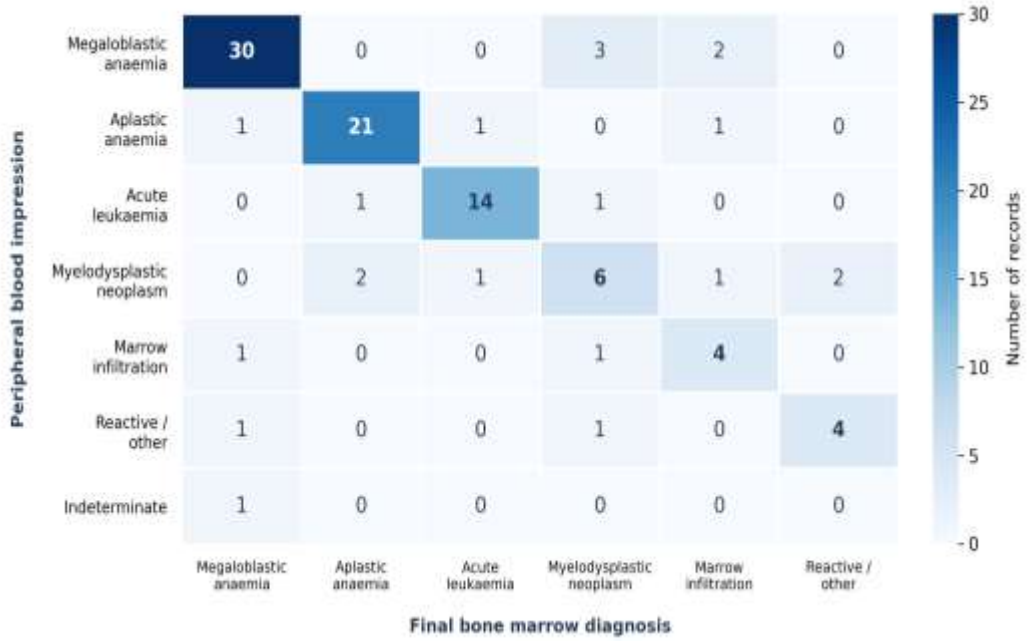


Figure 3. Agreement matrix comparing peripheral blood impressions with final marrow diagnoses in the dataset.

4. Discussion

The above allows comparison between blood results and bone marrow examination. Megaloblastic anaemia accounted for the highest proportion of diagnosed cases (34%), followed by aplastic anaemia (24%) and acute leukaemia (16%). This prevalence follows the trend observed by Porwal et al. where 58 out of 100 patients suffered megaloblastic anaemia (though the exact numbers are meaningless for epidemiological purposes). Similarly, Premkumar et al. detected megaloblastic anaemia to be prevalent among the diagnoses and documented a high rate of cobalamin deficiency, stressing the need to assess nutrition. As expected, macrocytes and hypersegmentation were prevalent in the group with megaloblastic anaemia, whereas blast cells prevailed amongst those with acute leukaemia and myelodysplasia. Marrow cellularity was set using such heuristics to ensure reproducibility and consistency of classification (Geetanjali and Das, 2019). Diagnostic frequencies can vary substantially across hospitals. For instance, Mohanty et al. found that the primary cause of pancytopenia in Southern Odisha was aplastic anaemia (unlike acute leukaemia), and Gajbhiye et al. noted prevalence of aplastic anaemia too. Those differences highlight the importance of patient sample bias. In this case example, white cells and platelets correlated positively with increasing marrow cellularity, whereas haemoglobin did not have any significant relationships. Calculations illustrate how correlations are calculated rather than prove their validity. Concordance rates between blood impressions and the assigned marrow diagnoses were relatively high at 79%, yielding Cohen's κ=0.729. Since both categorizations were determined artificially, clinical performance is non-existent. Yadav and Kumar stressed that identifying manageable conditions would benefit from thorough evaluation. Meanwhile, Jacob and Raj argued in favour of proper sampling in addition to clinical evaluation. Clinical work requires combining history-taking, examination, laboratory tests, blood smear microscopy and bone marrow analysis whenever required.

5. Conclusion

Based on the analysis, the prevalent diagnoses assigned were megaloblastic anaemia, aplastic anaemia and acute leukaemia. Morphology from peripheral blood matched various marrow diagnoses, whereas leukocyte and platelet numbers positively correlated with marrow cellularity. Agreement was at 79% (Cohen’s κ = 0.729).

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