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Original Research Article

PANCYTOPENIA: Epidemiological and Etiological Profile in Adult Patients of the Internal Medicine Department, CHU Hassan II, Fès.

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Abstract: ***Introduction*:** Pancytopenia is a fairly common hematological condition encountered in routine clinical practice. Since there is a wide variation in the etiologies of pancytopenia, even in different populations of the same geographical region, the identification of underlying etiologies is important. With this in mind, our study was undertaken to investigate the epidemiological and clinico-hematological profile of pancytopenic adults with the aim of identifying the different etiologies of pancytopenia. ***Materials and Methods*:** This is a retrospective study including all adult patients with pancytopenia admitted to the internal medicine department at Hassan II University Hospital in Fez, Morocco, from January 1, 2019 to December 31, 2022. Pancytopenia is defined by the simultaneous presence of a hemoglobin level < 13.0g/dL in men and 12.0g/dL in women, a total leukocyte count < 4.0 × 10^9 /L and a platelet count < 150 ×10^9 /L. Each patient included in the study underwent a series of investigations, including: blood count and reticulocyte count; peripheral blood smear examination; vitamin assays; bone marrow aspiration; immunophenotyping; osteomedullary biopsy (OMB) and serologies. Patients already diagnosed and under treatment, as well as patients under 18 years of age, were excluded from the study. ***Results*:** A total of 164 patients with pancytopenia were identified during our study period. The mean age of our patients was 48 years [extremes 18y-89y], with a preponderance of women (87women/77men). Mucocutaneous pallor was present in 100% of our patients, hepatosplenomegaly in 22.56% and hemorrhagic syndrome in 18.29%. Infectious syndrome and bone pain were observed in 12 patients (7.31%) and 05 patients (3.04%) respectively. Nineteen (19) patients had microcytic anemia, 85 had normocytic anemia and 60 patients had macrocytosis. Vitamin assays revealed vitamin B12 deficiency in 43 patients (26.91%), while 15 patients (9%) had folate deficiency. Combined B12 and folate deficiency was found in 5.48% of patients. Megaloblastic anemia was the most common etiology, accounting for 29.26% (48 patients), followed by hematological malignancies (23.78%, 39 cases), bone marrow hypoplasia (14.63%, 24 cases) and myelodysplastic syndrome (10.36%, 17 cases). In addition to these etiologies, we observed 7 cases of multiple myeloma, 2 cases of leishmaniasis and 2 cases of idiopathic thrombocytopenic purpura. In the remaining 25 cases, no specific bone marrow pathology could be identified. ***Discussion and Conclusion*:** Pancytopenia is an understudied entity in developing countries, despite its frequent clinical presentation. However, its occurrence remains an exceptional but particularly serious event due to the life-threatening anemic, hemorrhagic and infectious risks involved. A detailed clinical and hematological evaluation is essential to determine the underlying etiology of pancytopenia.

Keywords: Pancytopenia, Epidemiological Profile, Etiology.

INTRODUCTION

Pancytopenia is characterized by a concomitant decrease in red blood cells, white blood cells and platelets, resulting in anemia, leukopenia and thrombocytopenia respectively. This hematological condition is frequently observed in routine clinical practice. It is therefore not a pathological entity in its own right, but rather the manifestation of several underlying diseases and requires investigation. It should be suspected clinically when a patient presents with pallor, prolonged fever and a tendency to bleed [1, 2]. It can result from a variety of causes, indicating primary or secondary bone marrow damage. It is said to be of central origin when it is due to a quantitative or qualitative disturbance in bone marrow production. More rarely, it may be of peripheral origin, resulting from the destruction or extra-medullary sequestration of blood

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elements. In certain situations, the two mechanisms - central and peripheral - may be combined [2-5]. Indeed, the etiology of pancytopenia varies between populations according to differences in age composition, sex, nutritional status, geographical location, standard of living, exposure to certain drugs/toxins, exposure to infections and genetic and mutation profile [6]. Furthermore, data on the etiology of pancytopenia from various studies conducted in the same geographical region also differ due to differences in the methodologies used, the diagnostic criteria employed, the study period, the laboratory tests used and the department in which the study was conducted. Since the severity of pancytopenia and its underlying etiology determine its treatment and prognosis, it is important to identify the correct etiology to enable prompt and appropriate management specific to patients with pancytopenia.

With this in mind, our study was undertaken to investigate the epidemiological and clinico-hematological profile of pancytopenic adults, with the aim of identifying the different etiologies of pancytopenia.

MATERIALS AND METHODS

This is a retrospective study including all adult patients with new-onset pancytopenia admitted to the internal medicine department at Hassan II University Hospital, Fez, Morocco, during a 3-year period from January 1, 2019, to December 31, 2022.

Pancytopenia is defined by the simultaneous presence of a hemoglobin level < 13.0g/dL in men and 12.0g/dL in women, a total leukocyte count < 4.0 × 10^9 /L and a platelet count < 150 ×10^9 /L.

Each patient included in the study underwent a series of examinations, including: haemogram, reticulocyte count, bone marrow aspiration; peripheral blood smear examination.

Additional investigations were carried out according to diagnostic orientation, such as serum vitamin B12 and B9 assays, immunophenotyping, osteomedullary biopsy (BOM) and serological tests.

Previously diagnosed patients undergoing treatment (e.g. drugs, radiotherapy) and patients under 18 years of age were excluded from the study.

Patient information was collected from medical records and the hospital system (HOSIX). The results were then analyzed and statistics compiled using Excel software.

RESULTS

A total of 164 patients with pancytopenia were collected during our study period. The mean age of our patients was 48 years (extremes 18-89 years). The majority of patients were aged between 18 and 40, representing 37.20% of the total. Next, the 40-60 age group accounted for 31.71%, followed by patients aged over 60, representing 31.09% (**Table I**). There was a predominance of women, with an M/F sex ratio of 0.88 (87Women/77 Men).

Table I: Patient distribution by age group

Age group	Numbers	Percentages
[18-40 years]	61	37.20%
[40-60 years]	52	31.71%
>60 years	51	31.09%

Symptomatically, Mucocutaneous pallor was present in all our patients (100%), followed by hepatosplenomegaly with 22.56% (37 patients) and hemorrhagic syndrome with 18.29% (30 patients). Infectious syndrome and bone pain were observed in 12 patients (7.31%) and 05 patients (3.04%) respectively (**Figure1**).

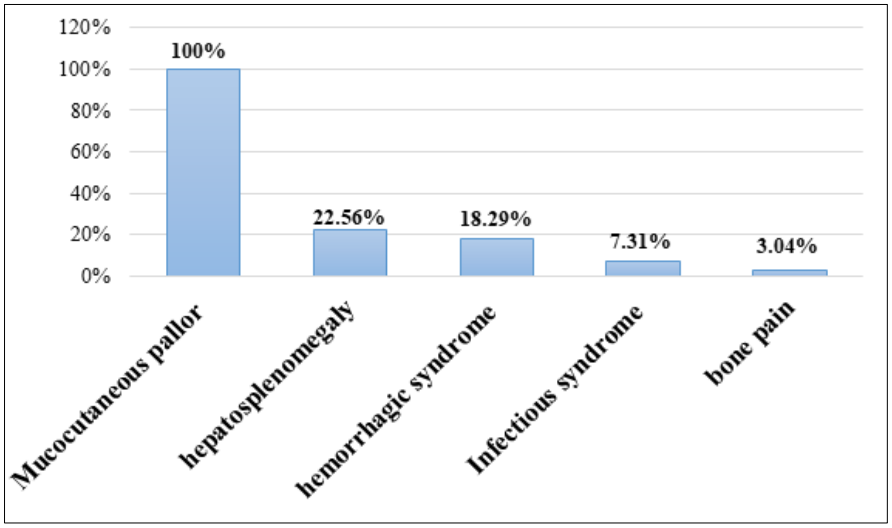

Figure 1: Distribution of patients by symptomatology

Hematological:

- **Mean hemoglobin: 6.21 g/dl [2.2 and 11.1].**
- **Mean platelet count: 48203.65/mm [2000 and 142000].**
- **Mean white blood cell count: 2108/mm3 [70 and 3930].**

Twenty-one patients had microcytic anemia (12.80%), 81 had normocytic anemia (49.40%) and 62 had macrocytosis (37.80%) (**figure2**).

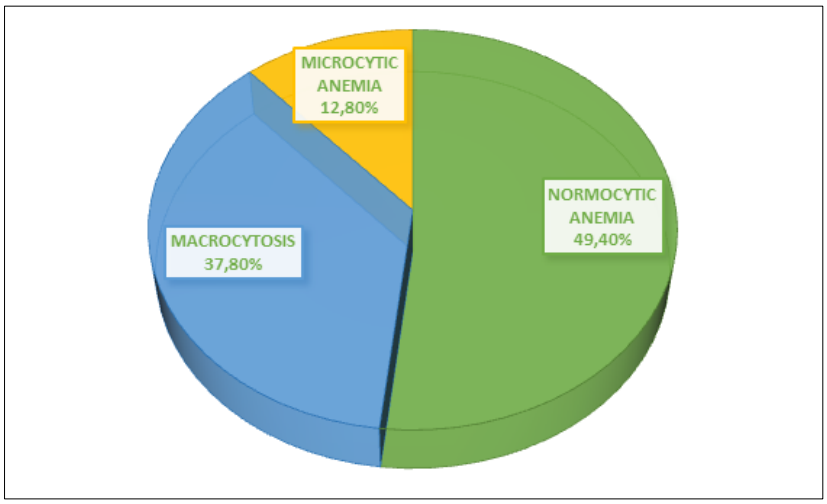

Figure 2: Distribution of patients by type of anemia

Vitamin assays revealed vitamin B12 deficiency in 43 patients (26.91%), while 15 patients (9%) had folate deficiency. A combined B12 and folate deficiency was found in 5.48% of patients (**Table II**).

Table II: Distribution of patients according to vitamin deficiency

Vitamin deficiencies	Numbers (n)
Vitamin B12	**43**
Vitamin B9	**15**
Combined deficiency B12+B9	**9**

The etiology of pancytopenia was identified on the basis of bone marrow studies and other complementary examinations. Megaloblastic anemia was the most frequent etiology at 29.26% (48 patients), followed by hematological malignancies at 23.78% (39 cases) (**see images 1a and 1b**), bone marrow hypoplasia at 14.63% (24 cases) and myelodysplastic syndrome at 10.36% (17 cases). In addition to these etiologies, we observed 7 cases of multiple myeloma, 2 cases of visceral leishmaniasis (**see images 2a and 2b**) and 2 cases of idiopathic thrombocytopenic purpura (**Figure3**).

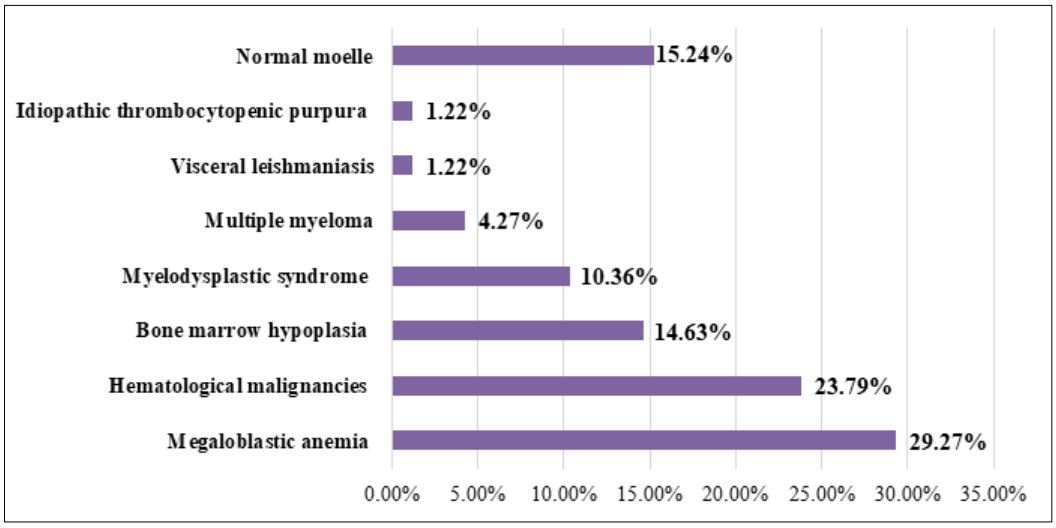

Figure 3: Patient distribution by etiology

For the remaining 25 cases, no specific bone marrow pathology could be identified.

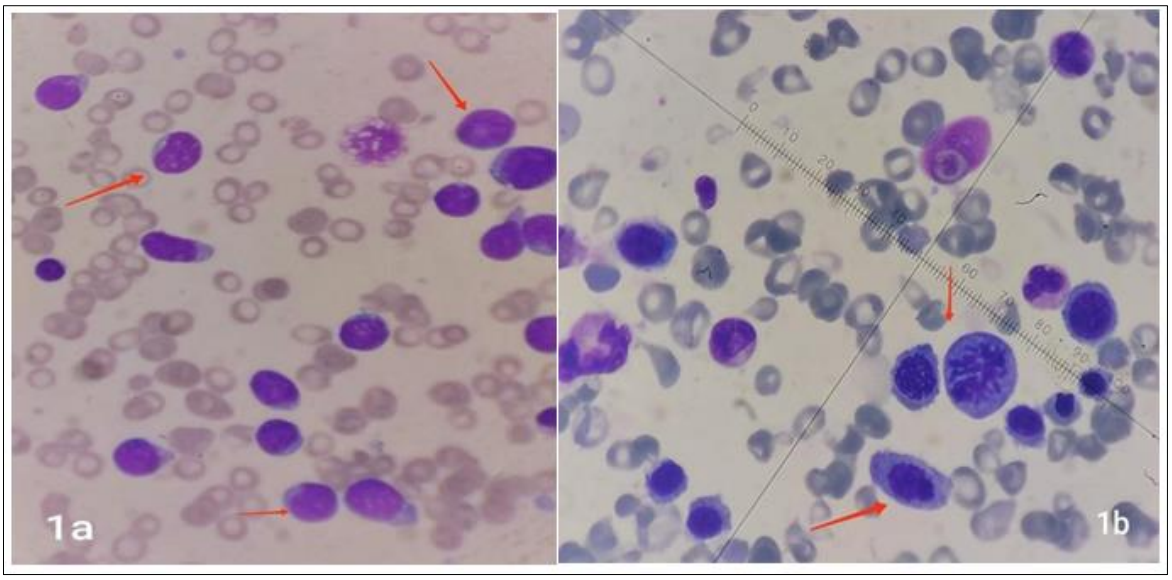

Image 1: Microscopic examination of bone marrow smear after May Grunwald Giemsa staining read under objective (×100) light microscope, showing blasts (1a) and megaloblasts with signs of dyserythropoiesis (1b)

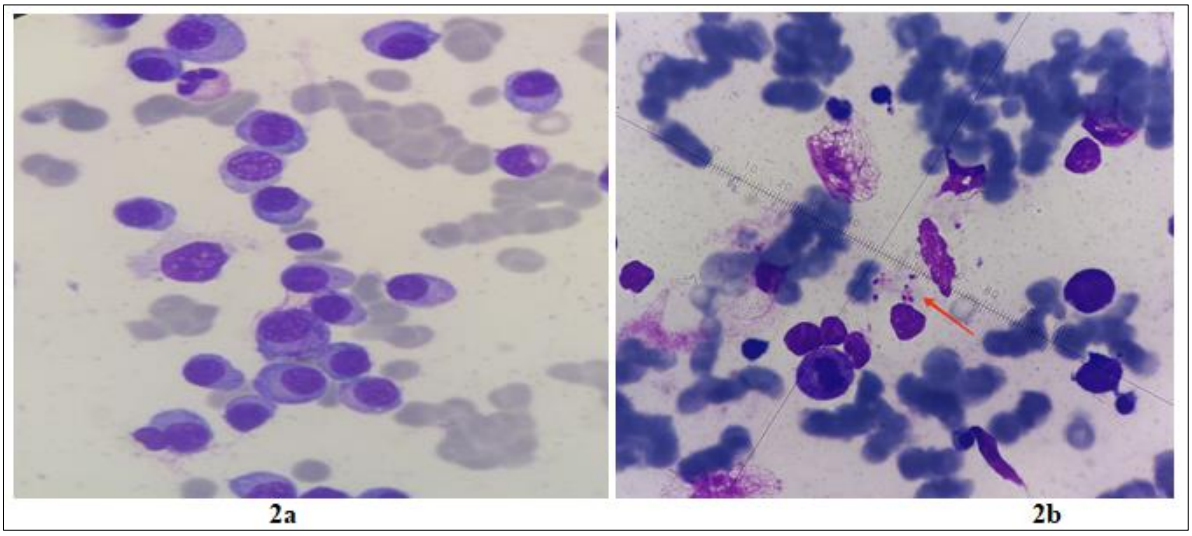

Image 2: Microscopic examination of bone marrow smear after May Grunwald Giemsa staining and objective reading (×100) under the light microscope, showing plasma cells (2a) and Leishman bodies (2b)

DISCUSSION

Pancytopenia is a very common hematological condition in clinical pathology, which can occur at any age. Symptoms may include fatigue, weakness, shortness of breath and an increased risk of infection and bleeding. To date, few studies have been carried out to assess the epidemiological and clinical profile of pancytopenia, or its underlying causes, so that patients can be properly managed.

The mean age of our patients was 48 years, with a predominance of the age group [18- 40 years], which accounted for 37.20%. This result is similar to those reported by Nabil *et al.*, in Morocco in 2012 and Kanté *et al*., in Conakry in 2019 [7, 8].

We noted a female predominance with a M/F sex ratio of 0.88. This female predominance was also reported by Kanté *et al.*, in Conakry in 2019 and by Kulkarni *et al*., in Karnataka in 2017 [8, 9]. In contrast, other studies of pancytopenia have shown a male predominance [7-10].

Anemic syndrome was observed in all patients. Similar observations have also been reported in other studies [10, 11]. Hepatosplenomegaly was observed in 22.56% of our patients. Similar incidences were also reported by Nabil *et al*., in Morocco in 2012 Mansuri et *al.*, in India in 2019 [7-10].

The vitamin assay confirmed 26.91% vit B12 deficiency and 9.14% folate deficiency. A combined vit B12 and folate deficiency was found in 5.48% of patients. Our results concur with those reported by several authors [12, 13]. The observed prevalence could be attributed to the often meat-deficient diet (the main

source of vitamin B12) and the common practice of overcooking food (which leads to folate destruction) in developing countries.

In our study, the etiological spectrum was dominated by megaloblastic anemia representing 29.26% of all cases. This is consistent with data reported in the literature. This prevalence in various other studies of pancytopenia ranges from 13.2% to 74% [9-19]. Vitamin B12 and/or folate deficiency correlated well with the diagnosis of megaloblastic anemia on marrow examination compared with other etiologies of pancytopenia. The high prevalence of megaloblastic anemia correlates with a high prevalence of nutritional deficiencies, i.e. vitamin B12 and folate [20]. These nutrients play an essential role in DNA synthesis. As a result, patients develop a disordered proliferation of red blood cells, white blood cells and platelets, which subsequently leads to pancytopenia and impaired immune function [21].

The second most common cause of pancytopenia was hematological malignancies, represented by 23.78% (39 cases) and consisting of acute myeloid leukemia (13.41%), acute lymphocytic leukemia (7.31%), plasma cell leukemia (1.82%) and acute Burkitt-type leukemia (1.24%). Vaidya also reported a similar prevalence of hematological malignancies; however, Jha *et al*., observed a higher percentage of hematological malignancies in their study [16-22].

Medullary hypoplasia accounts for 14.63% of all patients. A prevalence of between 18% and 21% has been observed in several other studies [23-25]. This difference may be explained by our sample size, which is smaller than theirs. Medullary hypoplasia is characterized by a failure of hematopoiesis, manifested by pancytopenia and a hypo-cellular marrow. Most cases are acquired and immune-mediated, but hereditary forms also exist. Environmental triggers include drugs, viruses and toxins, but most cases are idiopathic [26].

Myelodysplastic syndrome (MDS) is the underlying cause of pancytopenia in 10.36% of cases, with a similar prevalence observed in several studies [11-19]. In contrast, other studies have reported a lower rate of MDS myelodysplastic syndrome [6-17].

In this study, multiple myeloma, visceral leishmaniasis and idiopathic thrombocytopenic purpura (ITP) were uncommon causes of pancytopenia.

CONCLUSION

Pancytopenia is an understudied entity in developing countries, despite its frequent clinical presentation. Its occurrence remains an exceptional but particularly serious event, due to the life-threatening anemic, hemorrhagic and infectious risks involved. A detailed clinical and hematological evaluation is essential to determine the etiology of pancytopenia.

Bone marrow examination remains the gold-standard investigation for a complete evaluation of pancytopenia and to guide subsequent management of these cases.

Correct interpretation of the blood count and cytological study of the blood smear are essential to orientate the diagnosis and guide further investigations in the right direction.

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